OSHA

DOCKET H-122

OUTLINE

OF

TESTIMONY

DR. RICHARD CARCHMAN et al.

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INTRODUCTIONS

- Introduction of the panel.

- Our testimony will try to address and summarize our input contained in written comments concerning various aspects of the Proposed Rule on Indoor Air Quality.

- We hope to present the testimony in as succinct a manner as possible and if workable from a logistical standpoint, we may try to use slides. Tables and charts in the OSHA Proposed Rule and our written submission may be used.

- We have tried to outline the material that we hope to cover in this testimony.

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OUTLINE OF TESTIMONY

- Although we recognize that some nonsmokers may claim to be annoyed by tobacco smoke, the concerns and interests of both smokers and nonsmokers can be accommodated in an indoor environment by employing the indoor smoking option best suited to the particular space.

- We encourage individuals to show courtesy and mutual respect in accommodating their colleagues' wishes to smoke or not to smoke. We encourage the creation and maintenance of acceptable overall indoor air quality in workplaces and other indoor spaces, whether or not smoking occurs.

- If smoking occurs, we encourage the accommodation of the interests of both smokers and nonsmokers. Depending upon the nature of the indoor space and the interests of those using that space, options for indoor smoking may range from moderate, discretionary smoking throughout the indoor space to indoor smoking in designated smoking areas.

- Whether moderate, discretionary smoking occurs or whether smoking is limited to designated smoking areas, the scientific data indicate that nonsmoker exposure in properly ventilated indoor areas is either minimal or below existing detection

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limits. The data further indicate that it is has not been convincingly established that any chronic health effect is attributable to nonsmoker exposure to environmental tobacco smoke in the workplace.

- We respect the freedom of choice and encourage the accommodation of the interests and rights of both smokers and nonsmokers.

- The simple separation of smokers and nonsmokers, even under conditions of a shared ventilation system with the recirculation of air, is effective in minimizing nonsmoker exposures to ETS.

- Adequate ventilation will reduce complaints about indoor air quality, but it should be supplied to all spaces, regardless of smoking, for occupant comfort and well-being.

- Any requirement that smokers congregate in an enclosed space will place added demands upon a ventilation system, which may force the building owner or manager into often expensive, sometimes cost-prohibitive, reconstruction and maintenance of the air handling system.

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- In many instances, simple separation and adequate ventilation will provide similar reductions in exposures for nonsmokers.

- Smoking bans and severe restrictions on smoking, as proposed by OSHA, are unjustified by the data on ETS exposures in the workplace and public places, and restrictions such as those proposed by OSHA will do nothing to improve fresh air ventilation or reduce exposure to other substances in the indoor air. In this regard, we favor accommodation of the rights and interests of both smokers and nonsmokers in all workplaces covered by OSHA's Proposed Rule.

- The available scientific data do not convincingly support claims that exposure to ETS is associated with an increased risk of lung cancer, heart disease, respiratory disorders or other disease end points cited by OSHA. As a consequence, in our view, OSHA has failed from a scientific standpoint to establish significant risks of material impairment to worker health arising from exposure to ETS.

- This testimony will try to address the data which we believe support our position and the nature and extent of the scientific shortcomings reflected in the indoor smoking provisions of the Proposed Rule on Indoor Air Quality.

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- **OSHA fails to demonstrate a significant risk of material health impairment for <u>any</u> disease endpoint among nonsmokers reportedly exposed to ETS in the workplace.**

- **Particularly, OSHA fails to establish that <u>existing</u> exposures to ETS in the workplace pose a significant risk of material impairment to the health of nonsmokers.**

- OSHA's Proposed Rule states that "before the Secretary can promulgate any permanent health or safety standard, he must find that a significant risk of harm is present in the workplace and that the new standard is reasonably necessary to reduce or eliminate that risk."

- In an attempt to establish significant risk for ETS, the Proposed Rule reviews various disease endpoints reportedly associated with exposure to ETS, including (i) irritation, (ii) pulmonary effects (other than cancer), (iii) cardiovascular disease, (iv) reproductive effects, and (v) lung cancer.

- In addition, characteristics of mainstream smoke (the smoke to which the smoker is exposed) and sidestream smoke (the smoke

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from the burning tip of the cigarette) are enumerated, and a select number of studies on ambient exposures to ETS constituents in the workplace are examined.

- A form of risk analysis for both lung cancer and cardiovascular disease among nonsmokers in the workplace is presented. The risk analyses are based upon single, unrepresentative epidemiologic studies that are then applied to estimates of mortality for the total nonsmoking workforce in the U.S.

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- **No measured ambient exposure data for ETS are included in OSHA's estimate of risk due to exposure to ETS in the workplace.**

- OSHA's analysis of "significant risk" for ETS is based upon two epidemiologic studies in which ETS exposures are <u>not measured directly</u>. ETS exposures were estimated in the two studies by individual recall of exposure. Accurate quantitative measures of exposure cannot be ascertained through that kind of study.

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- Because no measured ambient exposure data for ETS are included in OSHA's estimate of risk due to exposure to ETS in the workplace, OSHA tries to offer an analysis of risk and a proposal for the complete elimination of ETS in the workplace without reference to any measured exposure data.

- However, studies that report measured data for constituents of ETS in the air of indoor work environments are, in fact, currently available.

- OSHA's discussion of such studies is limited, selective and unrepresentative of current ETS exposure data. Indeed, **OSHA's Proposed Rule does not reference a single ambient air monitoring study for the workplace published after 1991,** the same year in which OSHA admitted that it had no adequate data on "current levels of exposure" for ETS. [59 FR 15990-1]

- The Proposed Rule states that "estimating the risk from exposure to ETS requires the use of some measure of the extent of exposure." [59 FR 15997] OSHA acknowledges failure to integrate ambient ETS exposure data into its analysis of significant risk and states that "since there is no definition of, nor an established method for quantifying, exposure, it is not possible to determine a 'dose limit' that would eliminate significant risks." [59 FR 16001]

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- **OSHA's discussion of tobacco smoke constituents does not establish that ETS is carcinogenic.**

- OSHA's Proposed Rule on general IAQ does not include ETS because, according to OSHA, "the carcinogenicity of ETS discounts the use of general ventilation as an engineering control for this contaminant." [59 FR 15992] OSHA's attempt to demonstrate the "carcinogenicity" of ETS takes the form of an argument based on an analogy from mainstream smoke (the smoke to which the active smoker is exposed) to ETS. OSHA claims that ETS is chemically similar to mainstream smoke, and that "carcinogens" reportedly identified in mainstream smoke are also present in ETS. [59 FR 15979]

- The Proposed Rule presents a table of substances labeled "Table II-2: 43 Chemical Compounds Identified in Tobacco Smoke for Which There Is 'Sufficient Evidence' of Carcinogenicity in Humans or Animals." [59 FR 15979-80]

- **The 43 compounds listed therein are neither discussed nor reviewed in the Proposed Rule. Moreover, the Proposed Rule concedes that:**

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(1) Few of the substances identified as constituents of tobacco smoke (in the "list of 43") have been identified in ETS, i.e., "few of these individual [inhalational] constituents [imputed to ETS] have been identified and characterized." [59 FR 15987];

(2) The substances listed are also derived from other sources, i.e., "most of the identified carcinogenic components [in the list of 43] are not unique to ETS." [59 FR 15998]; and

(3) Individual substances responsible for the alleged "carcinogenicity" of tobacco smoke have never been identified, i.e., "the mechanism of carcinogenicity from exposure to ETS is not known." [59 FR 15998]

- OSHA's so-called list of "43 carcinogens in tobacco smoke" has been challenged in the scientific literature. One commentator notes:

> Many of these 43 MS [mainstream smoke] and/or tobacco components should be excluded from the list on the basis of published data on their tumorigenicity (or lack of it) in laboratory animals at levels determined in MS, their lack of tumorigenicity in most instances on inhalation, and the equivocal evidence of their tumorigenicity in humans at levels in MS. . . .

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> . . . Only five of the 43 components have produced respiratory tract tumors in laboratory animals exposed to the component via inhalation. Many have never been tested in an inhalation system. One component of great interest, 'benzo[a]pyrene,' has only produced lung carcinoma via inhalation in animals at an extraordinary massive dose, a finding classified as "equivocal." (RTECS, 1987).

- One of the few substances on the "list of 43" that has been tested via animal inhalation, nickel, has reportedly generated human-type lung cancers. However, nickel is derived from a number of sources.

- Nickel was tested for carcinogenicity at exposure levels far in excess of those found in the workplace, the environment or in tobacco smoke.

- It has been estimated that 40,000 cigarettes burning simultaneously in a 100 cubic meter enclosure would be required in order to generate a level of exposure to nickel equivalent to the Permissible Exposure Limit (PEL) established by OSHA.

- OSHA's "list of 43" was first developed in the 1970s, and it has been suggested that "many of the listed components are not relevant to those that would be found if the analysis were

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conducted on more recent cigarettes." This is particularly true of the substances dibenz(a,h)acridine and dibenz(a,h)anthracene. N'-nitrosonornicotine appears to be the only constituent characteristic of tobacco smoke from the "list of 43"; most of the constituents on the list, although theoretically identifiable, have never been identified in ETS (e.g., arsenic, chromium, etc.).

- Most of the substances on the "list of 43" were tested for carcinogenicity in animals through means other than inhalation.

- Skin painting of several components reportedly resulted in skin tumors, and neoplasms were reported in animals through ingestion and injection of various constituents. Several of the substances, e.g., benzene, formaldehyde and nitrosodiethylamine, reportedly produced neoplasms in areas other than the lung. (Epidemiologic studies of workers report increased risks of leukemia by benzene; liver cancer by vinyl chloride; and urinary bladder cancer by 4-aminobiphenyl and 2-naphthylamine.)

- Neither nicotine nor cotinine, the two substances selected by OSHA as biologic markers for exposure to ETS, are indicators

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of exposure to any of the constituents on the "list of 43." [59 FR 15974, 15991, 15998]

- Neither nicotine nor cotinine is itself a "suspect carcinogen."

- **OSHA concedes** that, since the constituents on the "list of 43" are not unique to ETS, "direct measurement of the carcinogenic components or related biomarkers in biological fluids would not provide a unique measure of exposure from ETS." [59 FR 15998]

- OSHA explicitly rejects one group of nine constituents on the "list of 43," the polycyclic aromatic hydrocarbons (PAHs), as candidate biomarkers precisely because they are found in low concentrations in tobacco smoke and because they are not unique to ETS. [59 FR 15998]

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- **Mainstream and sidestream smoke comparisons are not relevant to ETS.**

- The Proposed Rule presents two additional tables of constituents ascribed to tobacco smoke. [59 FR 15987-8] The

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tables provide a comparison of the amount of each constituent reported in mainstream smoke with the amount reported for the constituent in sidestream smoke (the smoke at the burning tip of a cigarette).

- OSHA's argument is that if constituent levels in sidestream and mainstream smoke are compared, quantities are greater in sidestream smoke. In our view, however, for purposes of OSHA's rulemaking, these comparisons to ETS are not relevant.

- **ETS is not the same as either mainstream or sidestream smoke. ETS is an aged and diluted mixture of sidestream and exhaled mainstream smoke; ETS is a dynamic, ever-changing mixture that undergoes chemical transformations and physical changes as it ages and is diluted in the air.**

- As one researcher in tobacco smoke chemistry has observed, "there are profound physical and quantitative chemical differences" among the three kinds of smoke (mainstream smoke, sidestream smoke and ETS). There are differences in physical and chemical properties and in relative concentrations of constituents.

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- **Studies indicate that constituents in ETS are <u>hundreds to thousands</u> of times more dilute than either sidestream or mainstream smoke.**

- Concentrations of ETS constituents in real-life situations are often below the limits of detection and measurement for even the most sensitive air monitors. Often, the contributions of ETS constituents to the ambient air are indistinguishable from background levels of the same constituents generated by other sources.

- OSHA's strategy of comparing mainstream and sidestream smoke ignores the profound effect of dilution in the ambient air upon tobacco smoke constituents. As two chemists report:

> The important question is not the ratio of sidestream/mainstream but rather what is the concentration of the constituent in the indoor environment and how does it compare to levels from sources other than ETS. Studies based solely on observations of fresh sidestream, are highly and unrealistically concentrated ETS should take into account the possible differences between these smokes and ETS found in real life situations.

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- **Elimination of ETS exposures in the workplace will not eliminate nonsmoker exposure to carcinogens; carcinogens**

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imputed to ETS by OSHA have permissible exposure limits, yet OSHA establishes a "no-exposure" standard for ETS.

- **OSHA's contradictory and insupportable position on ETS does not comply with OSHA's regulatory framework and undermines its own regulatory position on permissible exposure limits.**

- OSHA's Proposed Rule acknowledges that the ordinary air in the non-industrial workplace contains substances that have been identified as "carcinogens," whether or not smoking takes place. [59 FR 15983, 15998]

- The Proposed Rule presents a list of "typical pollutants" emitted from building materials, furnishings, appliances, office equipment and supplies. [59 FR 15984]

- Many of the same constituents contained in the Proposed Rule's list of "tobacco smoke constituents" are found in OSHA's tables for emissions from office furnishings and materials. [59 FR 15987-8; see Table I]

- Benzene, for example, is emitted by paints, wood preservatives, cleansers, disinfectants, fuels, solvents, etc.

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- Formaldehyde off-gases from particle board, pressed wood, resins, paneling, carpeting, upholstery, disinfectants, etc.

- Toluene is found in paints and other solvents, aerosol sprays, cleaners and disinfectants, air fresheners, fuels, etc.

- Benzo(a)pyrene is emitted from gas ranges, dryers, water heaters, and other combustion sources.

- Acetaldehyde, a substance in tobacco smoke described by OSHA as an "irritant," is found in adhesives, cosmetics and office supplies, and it emanates from other combustion sources. It also is an organic effluent that is emitted naturally by humans through metabolism.

- **OSHA's Proposed Rule therefore seeks to <u>eliminate</u> exposure to substances if they are derived from ETS, while seeking only to <u>reduce</u> levels of precisely the same substances if they are derived from sources other than tobacco smoke.** [59 FR 16016, 16023-16027]

- Obviously, given the foregoing, **complete elimination of ETS will not eliminate exposure to substances imputed to it.** OSHA cannot argue that the contribution of ETS to substances in the air of workplaces is "different" from, or greater than,

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contributions from other sources because OSHA does not present data on either ETS constituent levels or levels of constituents from sources other than ETS.

- The elimination of ETS in the workplace cannot be achieved under OSHA's own regulatory framework. OSHA argues that tobacco smoke contains carcinogens and that no exposure to it should be permitted. The list of constituents imputed to ETS by OSHA [59 FR 15979-80] contains suspected carcinogens currently regulated by OSHA through permissible exposure limits (PELs) (e.g., arsenic, benzene, chromium, nickel, formaldehyde, benzo(a)pyrene, etc.). [See Tables II-IV] OSHA cannot use substances with permissible exposures to demonstrate the "carcinogenicity" of ETS, and, at the same time, argue for its elimination.

- For the same reasons, OSHA cannot restrict its IAQ proposal to only the non-industrial workplace, while applying its de facto smoking ban to all workplaces, including both industrial and non-industrial venues.

- For the industrial worker, OSHA's plan affords no protection from ordinary indoor air quality constituents found in the work environment. This means that the nonsmoking industrial worker, under OSHA's Proposed Rule, may be exposed to levels

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of chemicals 100 to 1,000 times greater than those found in either the non-industrial workplace or in ETS while, at the same time, the worker is not to be exposed to even a single wisp of tobacco smoke. From a scientific standpoint, this position is ludicrous and clearly displays OSHA's policy objective for the elimination of smoking at all costs.

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- **OSHA's examination of workplace exposure studies on ETS is selective, the studies are outdated and are not representative of current ETS exposures in the workplace, and the data from the Proposed Rule's discussion of ETS workplace exposures are not used in the determination of "significant risk" from ETS.**

- OSHA's analysis of the data "available for . . . assessing exposure to ETS in the workplace" purports to establish average indoor levels of ETS and the percentage of average daily ETS exposure for nonsmokers in the workplace. [59 FR 15987-91]

- The Proposed Rule discusses a select number of studies that measure nicotine and respirable suspended particulates as markers for ETS in the air of workplaces. The studies are used to determine a range of average exposures to ETS. Four

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"human activity pattern studies" are used to establish OSHA's claim that the "workplace is a major location of ETS-exposure to nonsmokers." [59 FR 15990]

- **The studies used in the Proposed Rule's discussion of ETS exposures are neither representative of, nor generalizable to, current levels of nonsmoker exposure in the workplace.**

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- **Human activity pattern studies for assessing workplace exposures to ETS are misinterpreted in the Proposed Rule. Such studies are inherently inaccurate and are not representative of current workplace exposure patterns.**

- Human activity pattern studies are based upon an individual's recall of ETS exposure over a given period of time. Estimates of exposure are acquired through questionnaire responses and diary entries of study participants. Both the accuracy and the quantifiability of such "data," when compared to actual measures of ETS constituents in the air, have been challenged. (e.g., Ex. 8-66, Coultas, et al.)

- Two of the four human activity pattern studies cited in the Proposed Rule were conducted in the mid-1980s. Data for the

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third cited study were gathered in 1990, and a fourth study cited by the Proposed Rule is undated. [59 FR 15988-90] The generalizability of the sample populations in each of the respective studies to the entire U.S. workforce under current exposure conditions is not addressed in the Proposed Rule.

- The first study cited in the Proposed Rule is the California Activity Pattern Survey (CAPS), conducted in 1987-88. [59 FR 15989]

- The Proposed Rule suggests that the California study indicates that "the most powerful predictor of potential exposure to ETS" is the workplace. OSHA claims that the study establishes that "77 percent of males and 85 percent of females were exposed [in the workplace] an average of 313 minutes and 350 minutes, respectively." [59 FR 15987]

- Close examination of the study itself and a subsequent published report [Ex. 8-168] indicates that the exposure time reported was not actual or continuous but total potential exposure time. The study indicates that while 62 percent of the sample population responded that they were in the presence of smokers at some time during the day, only 27 percent were in work locations with smokers. The Proposed Rule fails to mention these important qualifications.

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- The Proposed Rule also does not discuss a more recent study of human activity patterns among Californians conducted by the U.S. EPA (1993).

- Exposures to ETS were assessed in precisely the same way as in the CAPS study, namely, by personal recall diary. The study concludes that "less than 2 percent of the time was spent indoors or in transit in the presence of smokers." The report also notes that personal exposures to particles (daytime averages) did not differ significantly between individuals who reported exposure to ETS and those who did not.

- The second population survey mentioned in the Proposed Rule is an undated study, the National Health Interview Study, conducted by the U.S. Centers for Disease Control (CDC). [Ex. 8-51] According to the Proposed Rule, the "results suggest that at least 19 percent of employed nonsmokers experience ETS exposure at work." [59 FR 15989]

- The Proposed Rule characterizes the data in the CDC study as an "underestimate" because they are "based solely on self-reported information and the question was not very specific in defining immediate work area." [59 FR 15995] This criticism, of course, applies to all the human activity pattern surveys

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relied upon by OSHA in its analysis of workplace ETS exposures.

- A "re-analysis" of a 1986 study is cited as the third human activity pattern survey in the Proposed Rule. [Ex. 8-67; 59 FR 15989, 15995] The original study reported that the workplace was a source of ETS exposure for only 28 percent of all respondents. According to the Proposed Rule, a "re-analysis" of a subset of the data from the Cummings, et al. study purportedly indicates that 49 percent of employed subjects (who report no ETS exposure at home) report ETS exposure at work. [59 FR 15989] OSHA concludes from this that the workplace is a significant source of ETS exposure for nonsmokers. [59 FR 15989] OSHA in fact adopts the 49 percent exposure figure as its upper bound estimate for nonsmoker exposure to ETS in all U.S. workplaces. [59 FR 15995] Again, the applicability of those data -- compiled in 1986 -- to the entire nonsmoking workforce, is not addressed.

- The fourth human activity study cited in the Proposed Rule was conducted in 1990 and is offered in support of OSHA's contention regarding "the widespread" exposure to ETS in the workplace. [Ex. 8-98] The survey included 196 nonsmoking volunteers who provided estimates of their respective exposures to ETS during the work day. According to the

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Proposed Rule, the study indicates that more nonsmokers are exposed to ETS at work than at home. [59 FR 15989]

- The Proposed Rule does not mention, however, that the volunteers for the study were recruited only from workplaces that permitted smoking. The sample obviously was not randomly selected and therefore cannot serve as the basis for OSHA's claim regarding the magnitude of ETS exposure in the workplace. Interestingly, the study also reports average exposures to ETS of approximately 30 minutes per day. Those data directly contradict OSHA's interpretation of exposure time from the CAPS study (350 minutes of ETS exposure a day). [59 FR 15989]

- **Overall, the four "human activity pattern studies" selected by OSHA do not provide a consistent or complete dataset for estimating the extent of nonsmoker exposure to ETS in the workplace. The data are unverified by actual exposure measures and are not representative of <u>current</u> exposure conditions for ETS in the workplace.**

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- **The failure to utilize current data on ETS exposures in the workplace invalidates OSHA's conclusions that "the workplace**

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is a major location of ETS exposure to nonsmokers" and that "exposure to ETS is pervasive." [59 FR 15990, 16007]

- OSHA's analysis of "significant risk" for ETS assumes that the proportion of nonsmoking workers exposed to ETS in the workplace remains constant over time. [59 FR 15996] That assumption is invalid.

- Changing patterns of smoking, decreased percentages of smokers, increased numbers of smoking restrictions and improved ventilation in the workplace will all affect estimates of nonsmoker exposure to ETS.

- **For an accurate representation of ETS exposure, OSHA must therefore determine (1) how many smokers are employed; (2) how many are permitted to smoke at work and under what conditions; (3) how many worksites are adequately ventilated; (4) and how (1)-(3) will affect actual ambient exposures to ETS. The Proposed Rule does not address any of these conditions.**

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- **The Proposed Rule's discussion of ambient levels of ETS constituents in the workplace is selective and incomplete; the**

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studies cited are outdated and unrepresentative of current exposure levels reported for ETS in the workplace.

- The Proposed Rule discusses a small and select group of ETS measurement studies from homes and other venues in order to provide an average estimate of ETS concentrations in the workplace. [59 FR 15990-1] The studies cited by OSHA employ nicotine and respirable suspended particulates (RSP) as markers for ETS exposures.

- According to OSHA's analysis, studies in offices report "a range of average nicotine concentrations" of 2 to 10 micrograms per cubic meter (ug/m), and a range for RSP exposures of 18 to 95 ug/m. [59 FR 15990] The "average" exposure for nicotine is later "adjusted" to "5 to 10 ug/m" for the average worker and "50 to 100 ug/m" nicotine for the most-exposed individuals. [59 FR 15991]

- **The Proposed Rule cites no published studies on ambient nicotine or RSP measures in the workplace after 1991. This omission includes two major literature reviews on the issue of ETS markers and measurement.**

- Other pre-1991 studies on nicotine and RSP measurements in the workplace, involving hundreds of offices and restaurants, are

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not considered in OSHA's analysis. The latter studies, together with studies on other markers for ETS exposures in the workplace, were, however, submitted to the docket of the OSHA RFI on Indoor Air in 1992. [Ex. 3-1074]

- The studies on ambient measures of nicotine in offices and restaurants that were omitted from OSHA's analysis report average levels of approximately 2.0 and 3.5 ug/m nicotine, respectively. These exposures are equivalent to 1/400 to 1/200 of the nicotine found in a single cigarette. Averages for nonsmoking areas in workplaces with smoking restrictions are even lower, averaging less than 1 ug/m nicotine, or about 1/1,000 of the nicotine in a single cigarette.

- **This means that the typical nonsmoking worker would have to spend from 200 to more than 1,000 hours in an office, restaurant or public place in order to be exposed to the nicotine equivalent of a single cigarette.**

- Respirable suspended particulates (RSP) are contributed by a number of sources, a point acknowledged in the Proposed Rule. [59 FR 16003] OSHA states:

> People contribute millions of particles to the indoor air primarily through the shedding of skin scales. Many of these scales carry

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microbes, most of which are short-lived and harmless. Clothing, furnishings, draperies, carpets, etc. contribute fibers and other fragments. Cleaning processes, sweeping, vacuuming, dusting normally remove the larger particles, but often increase the airborne concentrations of the smaller particles. Cooking, broiling, grilling, gas and oil burning, smoking, coal and wood generate vast numbers of airborne indoor pollutants in various classifications.

- Results of a 1993 study on particle exposures conducted by the U.S. EPA indicate that one hour of cooking activity generates approximately 100 times the particle concentration from a single cigarette. The study reported that average percent contributions from "fine particle mass" (RSP) were: 10 percent from smoking, 68 percent from outdoor sources and 22 percent from unidentified sources.

- Special methods have been developed for the analysis of airborne particles that determine the relative contribution of ETS to total particles in the indoor air. One analytic technique employs ultraviolet particulate matter (UV-PM) as an indicator of the particle fraction contributed to the air by ETS.

- Studies of UV-PM measurements in offices report ranges of from 27 to 44 ug/m in areas where smoking is permitted. Although indoor exposure limits do not exist for ETS-related particles,

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the World Health Organization has designated 100 ug/m or less as an exposure level of "limited or no concern" for particles contributed by ETS.

- A recent review has summarized average levels of airborne particles from smoking and nonsmoking areas reported in studies performed in various settings. The average particle concentration in the air of homes with smokers is about 27 micrograms per cubic meter higher than in homes of nonsmokers; offices and public places that permit smoking report average levels of particles that are about 22 micrograms/cubic meter higher than those reported for nonsmoking locations, and smoking areas of restaurants report levels that are 42 micrograms/cubic meter higher, on average, than nonsmoking areas.

- In the largest single study of its kind, researchers monitored 585 offices for various ETS-related constituents, including particles. The average level of particles recorded for 331 offices in which smoking was permitted was 46 ug/m, compared with an average of 20 ug/m for 254 nonsmoking offices. The difference of 26 micrograms per cubic meter represents a level of particles that is far below that designated by the WHO as of "limited or no concern."

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- The Proposed Rule contends that the contribution of RSP by smoking is much greater than that reported in studies employing the UV-PM method.

- The Proposed Rule combines the results of three studies of smoking and nonsmoking buildings conducted in the early 1980s. The combination of data from the three studies provides an average estimate of 262 ug/m RSP in smoking buildings, compared with 36 ug/m in nonsmoking buildings. [59 FR 15990] An analysis identical to that presented in the Proposed Rule occurs in a 1992 paper written by two antismoking activists. (The paper, however, is not referenced in the Proposed Rule.)

- Close examination of the three studies cited by OSHA reveals that the data therein do not support the contention of the Proposed Rule.

- One of the studies measured RSP levels in pizzerias, bars, lodge halls, bowling alleys, church bingo games and fast food restaurants in 1980. The only office measurement reported was conducted under experimental conditions in a room in which levels of ETS were generated by seven smokers smoking 32 cigarettes in 49 minutes, yielding RSP values as high as 500 micrograms per cubic meter. One of the other studies cited

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included no office measurements. The studies clearly do not represent typical 1994 workplace levels of ETS exposure.

- According to a comprehensive review undertaken by researchers at Oak Ridge National Laboratories, "chemical means for estimating the contribution of ETS to RSP have been evaluated, and suggest that ETS-RSP may comprise from 10 percent to 50 percent of indoor air RSP, in the field scenarios to which the methods have been applied."

- Even a cursory examination of actual studies, consisting of hundreds of office, restaurant and other workplace situations, reveals that source-apportioned RSP levels due to ETS are at levels 5 to 10 times lower than those suggested in OSHA's Proposed Rule.

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- With the exception of nicotine, none of the substances used as markers for ETS in the air are characteristic of tobacco smoke.

- Other sources such as heaters, stoves, building materials, cleaning products and human activities often generate greater levels of those substances than ETS. For example, studies

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indicate that automobile combustion, industrial processes, home heating and gas cooking are the predominant sources of carbon monoxide and nitrogen oxides in indoor air.

- For this reason, neither constituent is an appropriate marker for ETS. Researchers report that there is little difference in ambient levels of carbon monoxide or nitrogen oxides in smoking and nonsmoking areas of workplaces and public places and in homes with or without smokers. Levels of volatile organic compounds such as formaldehyde and benzene in the presence of smoking are often indistinguishable from levels reported in nonsmoking areas. Studies that have examined ETS constituent levels of nitrosamines also report minimal contributions to overall ambient air levels in homes, offices and public places.

- Nicotine and RSP were selected by OSHA as the most suitable markers for assessing exposure to ETS. While nicotine is characteristic of tobacco smoke in the ambient air, it represents a gas-phase constituent and indicates nothing about the particle phase of environmental tobacco smoke.

- RSP, on the other hand, is not characteristic of tobacco smoke, but, if correctly sampled and analyzed, can provide approximations of exposure to the particle phase of ETS.

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Measurements of both nicotine and RSP are typically reported in terms of micrograms per cubic meter (ug/m).

- The absolute values of the levels measured, however, may not be meaningful to anyone other than scientifically trained personnel. It is therefore convenient to refer to a comparative or illustrative device in order to facilitate understanding about the levels of exposure to nicotine and RSP as reported in the scientific literature.

- **One particularly useful illustrative means for representing reported levels of nicotine and RSP in the ambient air is the notion of "cigarette equivalents."**

- The use of "cigarette equivalents" as a device for understanding ETS exposures does not imply that active smoking and nonsmoker exposure to ETS are the same thing, or that mainstream smoke is "equivalent" to ETS. Nor does it mean that a measure of nicotine or RSP in terms of "cigarette equivalents" represents exposure to other constituents in ETS.

- The concept of "cigarette equivalents" offers a convenient means for quantitative comparisons of ETS exposures and is a commonly used method for reporting measured levels in the published literature.

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- For example, Oldaker, et al. reported average levels of nicotine exposure of 4.8 ug/m for 125 offices. The authors estimated exposures to nicotine for an eight-hour work day in an office to be equivalent to 0.02 of a cigarette. The authors also measured nicotine levels in 82 restaurants and the resulting average concentration was 5.1 ug/m; the exposure equivalent for a one-hour meal was 0.003 of a cigarette.

- Carson and Erikson, cited in OSHA's Proposed Rule [59 FR 15991], measured nicotine and RSP (UV-PM) in 31 offices. The authors wrote: "Exposure estimated from mean nicotine and UV-PM results were 0.004 and 0.001 cigarette equivalent per hour, respectively."

- Proctor measured nicotine levels in smokers' offices and reported that the average level of 3.1 ug/m nicotine would provide an exposure equivalent of 0.018 to 0.010 of a cigarette over the course of a work-day. Proctor writes: "This means that a male nonsmoker would have to work in the smoker's office for over 11 weeks before being exposed to the equivalent nicotine as from smoking one cigarette." UV-PM/RSP levels in smokers' offices were reported at 24 ug/m. This would translate into an exposure equivalent of 0.013 cigarettes per day.

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- Proctor writes: **"This again would result in a male nonsmoker working in the smoker's office for 15 weeks before being exposed to the equivalent particulates as smoking one cigarette."**

- Hinds and First, in one of the first studies of its kind, measured nicotine levels in various public places in 1975. The venues included waiting rooms, restaurants, and cocktail lounges. Measured levels of nicotine averaged ranged from 1.0 to 10.3 ug/m, translating into equivalents of 0.001 to 0.009 cigarette per hour.

- In 1993, Hedge, et al. measured nicotine in 27 air-conditioned offices under various smoking policies. The authors write: "[A] nonsmoking office worker in open offices who does not spend time in designated smoking areas on average may be exposed to the nicotine content of about three cigarettes per year."

- **Although a suitable internal dose marker for ETS is not available, scientists have estimated that ETS-related particle uptake in the typical nonsmoker is approximately two-hundredths of one percent (0.02 percent) that of the active smoker.**

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- **Other scientists have estimated that ETS "inhaled doses" (based on particles) are 10,000 to 100,000-fold less than average doses calculated for active smokers. The estimated nonsmoker "dose" is equivalent to actively smoking less than one cigarette over the course of a year.**

- Another scientist recently calculated estimated "retained doses" for nonsmokers using average exposures to various ETS constituents reported in the published literature. The calculated dose for tobacco smoke particles, expressed in terms of cigarette equivalents, ranges from less than one-half to about four cigarettes per year for "light" and "heavily-exposed" nonsmokers, respectively.

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- **The Proposed Rule does not utilize actual ambient exposure measures for ETS in the workplace in its determination of "significant risk." Exposure estimates from epidemiologic studies on ETS are used in the determination of "significant risk." Exposure estimates from epidemiologic studies are not quantifiable; they are unreliable and inconsistent with actual ambient measurements of ETS.**

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- In its analysis of "significant risk" for ETS, OSHA employs two epidemiologic studies on lung cancer and heart disease in nonsmokers. [Exs. 8-106, 8-139; 59 FR 15995] Exposures to ETS were determined in those studies through the use of questionnaires that, in turn, were dependent upon the accuracy of recall of exposure among those questioned. **No actual ambient exposure measures were included in the epidemiologic studies.**

- **OSHA's entire discussion of ambient measures of ETS exposures in the workplace is omitted from its significant risk analysis and replaced by the exposure estimates from two epidemiologic studies on nonsmoker lung cancer and heart disease.**

- One critical source of bias in epidemiologic studies on ETS is called "exposure misclassification bias" and arises from errors in reporting ETS exposures.

- Epidemiologic studies do not measure <u>actual</u> ETS exposures, but rather employ questionnaires to generate estimates of ETS exposure over long periods of time. Sometimes, the studies use exposure estimates given by spouses, children, or next-of-kin. The questionnaires used in epidemiologic studies on ETS vary and have not been validated or checked for accuracy.

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- The National Research Council and other authors have criticized the use of questionnaires as representations of accurate and comprehensive exposure histories in ETS studies. Other studies demonstrate that questionnaires are an unreliable and inaccurate measure of ETS exposure.

- Typically, questions regarding ETS exposures in epidemiologic studies are of the following sort: "Are you married to a smoker?"; "How long have you lived with a smoker?"; "About how many cigarettes a day did the smoker smoke in your presence?"; "About how many cigarettes a day did the smoker smoke?"; etc. Answers to such questions vary widely across studies.

- For example, Friedman, et al. noted that, in their study, 30 to 35 percent of nonsmokers who were married to smokers reported no exposure whatsoever to ETS.

- A more recent study reported a 36 percent exposure misclassification rate when ETS exposures determined by questionnaires were compared to exposures determined by ambient air measurements. The authors of that study conclude: "The results . . . suggest that questionnaires lead to a large amount of misclassification which must be taken into account when assessing the effect of ETS exposure" and that "an

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objective method to measure exposure which is sensitive, accurate, and reliable is needed to validate them."

- Another recent study that compared ETS measurements with questionnaire responses found that "the false report rate was high. Among those 575 participants reporting an average of 42 or more hours/week [exposure to ETS], 58 percent did not have a detectable cotinine level." Coultas, et al., in a study cited in the Proposed Rule [Ex. 8-66], report that "the levels of cotinine, respirable particles, and nicotine varied widely with self-reports of exposure to ETS."

- A second study by Coultas, et al. reports that "personal exposure also varies with the nonsmoker's proximity to the smoker. Questionnaires cannot comprehensively and accurately assess each of these factors. Not surprisingly, we found that the questionnaire responses were poor predictors of concentrations of respirable particles and nicotine."

- Schenker, et al., in another exposure assessment study, concluded that "self-reported exposure to ETS is an inaccurate measure of passive smoking in the occupational setting." Schenker, et al. noted in their study that "responses to initial screening questions used to detect a person's exposure to passive smoke were more reliable for residential than for

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occupational exposure . . . [Q]uantitative measures of exposure to passive smoke, i.e., number and duration of exposure, were even less reliably reported."

- In another study by Coultas, et al., the authors reported that "responses concerning recent tobacco smoke exposure and urinary cotinine levels were correlated only to a modest degree." The authors "conclude that adults can reliably report whether household members smoked during their childhood, but information on quantitative aspects of smoking is reported less reliably."

- Lerchen and Samet in 1986 reported that spouses of smokers correctly reported the smoking status of their spouses, however, "for the number of cigarettes smoked per day, wives tended to report 20 cigarettes smoked even when their husband smokes substantially more or less." OSHA argues, within the context of its analysis of "significant risk" for ETS, that home "exposures" to ETS are comparable to workplace exposures. It is argued that "in the absence of purely occupational data, information derived in environments other than worksites is also considered." [59 FR 15994]

- The Proposed Rule cites a report prepared by Meridian Research in 1988 that contends that "it is the exposure to

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environmental tobacco smoke, and not the environment in which that exposure occurs, that is the important risk factor." [Ex. 8-221]

- The Proposed Rule continues: "Therefore, health effects observed and the risk estimates calculated from studies of the general population, or of selected subgroups, such as nonsmoking wives of smoking husbands, are relevant to the working nonsmoking population." [59 FR 15994]

- There are at least three distinct issues regarding OSHA's argument. First, OSHA equivocates on the phrase "exposure data." OSHA proposes to replace actual ambient air measures of ETS constituents in the workplace with exposures assessed by questionnaire responses in epidemiologic studies.

- **It is clear, however, that questionnaire responses cannot quantitatively approximate, much less replace, actual measures of ETS constituents in the air of workplaces.**

- The second issue raised in OSHA's argument concerns the comparability of actual levels of ETS constituents in the home and in the workplace. OSHA contends (but does not prove) that the levels are comparable. [59 FR 15994] Recent data, however, indicate that this is not the case.

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- In a 1993 study of 96 nonsmoking, married women, ETS exposures were continuously monitored over a one-week period. The results for actual measures of ETS exposures (using 3-ethenylpyridine and nicotine as markers for ETS) indicate that workplace exposure is "tenfold lower than home exposure due to living with a smoker."

- Average values for exposure to nicotine in the workplace indicate that it is a trivial source of (ETS) exposure (median value, 0.21 ug/m nicotine, compared to the nicotine delivery of a single cigarette: 880 ug/m. The third issue raised in OSHA's argument is whether or not data from household "exposures" to ETS can be applied to the workplace.

- If current published data regarding workplace exposure to ETS constituents were not available, then perhaps OSHA could make its argument. However, current workplace exposure data are available, including seven major studies and two major review surveys of ETS measurements in workplaces, that could have been used by OSHA in its analysis.

- OSHA chose <u>not</u> to use the data from those studies and reviews because, in most instances, the data reveal that ETS exposures in the workplace are minimal and often indistinguishable from background levels.

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- Even in the complete absence of appropriate data on ETS measurements in the workplace, OSHA would still have to justify its argument for the application of exposure data from epidemiologic studies in the home to the workplace.

- As one scientist notes:

> Because workers not exposed to ETS and workers exposed to ETS in the same occupational group have not been medically followed for several years, there is no justification to apply the reasoning that because home exposure through spousal smoking might be associated with cardiopulmonary disease, then workplace ETS exposure can be expected to have a similar association . . . . Results of household exposure cannot be applied to workers . . . . Confounding factors related to ETS exposure in workplaces are different from factors influencing spouses and children in studies of household exposure. Dietary factors and household pollution may influence the incidents of spousal and childhood diseases. On the other hand, workers are exposed to industrial chemicals and outdoor pollutants as well as work-related stress. Familial patterns of inherited or acquired susceptibility to cardiopulmonary disease do not apply to occupational groups . . . . Unlike household exposure, workplace exposure can be monitored by good industrial hygiene practice.

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LUNG CANCER

- **OSHA'S Proposed Rule fails to demonstrate that current ETS exposures in the workplace pose a significant risk of material health impairment due to lung cancer in exposed workers.**

- Due to its failure to focus on the best available data on workplace ETS exposures and to its numerous errors and omissions, OSHA's Proposed Rule does not adequately demonstrate a significant risk of material health impairment due to lung cancer in persons exposed to ETS in the workplace.

- **OSHA fails to adequately support the position that ETS exposure in the workplace is causally associated with lung cancer in nonsmokers.**

- OSHA claims [[at Section II.C.6.(a) (59 FR 15979)]] that data from epidemiologic studies, "taken in the aggregate," support a causal association between ETS exposure and nonsmoker lung cancer. OSHA does not provide references in support of this claim.

- In subsequent text, OSHA references the 1992 EPA Risk Assessment on ETS [Ex. 8-311] for that report's discussion of <u>active smoking</u> studies. OSHA invokes the argument of

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"biological plausibility," suggesting that unspecified qualitative similarities between mainstream smoke and ETS support an analysis of cancer risk allegedly due to exposure to the latter.

- This argument does not withstand critical analysis, such as recognition of the distinct chemical differences among mainstream smoke, sidestream smoke, and ETS detailed elsewhere in this submission. OSHA's failure to differentiate among different forms of tobacco smoke pervades this section of the Proposed Rule.

- The EPA Risk Assessment on ETS suggested that, because mainstream smoke reportedly contains over 40 "known" or "suspect" carcinogens, so must ETS. [Ex. 8-311] However, the EPA's claim is not convincingly supported by scientific data.

- The EPA concedes in its report that specific substances responsible for the supposed carcinogenicity of mainstream smoke have never been identified, and that associations between "suspect" carcinogens in mainstream smoke and specific diseases have never been established.

- Moreover, most of the claimed "carcinogens" in mainstream smoke have never been tested via inhalation in animals.

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- OSHA references a study by the U.S. Centers for Disease Control (CDC), which reported that cotinine, a metabolite of nicotine, was detected in samples of bodily fluids of all the persons surveyed in the study. [Ex. 8-50] OSHA interprets these reported results as "indicating that everyone in the sample had detectable exposure to tobacco smoke." [59 FR 15980]

- It is an oversimplification to assume that any detectable level of cotinine in bodily fluids necessarily implies exposure to tobacco smoke. Nicotine is also present in several foods (potatoes, tomatoes, eggplant, tea); detectable cotinine levels may be produced following the ingestion of reasonable amounts of these foods. At the sensitive levels of detection employed in the CDC paper (to 0.030 ng/mL), cotinine related to dietary nicotine could certainly be detected.

- **Therefore, any extrapolation of these reported results to the classification of persons as "exposed" to ETS should take diet into account, rather than immediately presuming that detectable cotinine must be due to ETS exposure.**

- **OSHA'S reliance on data on "spousal smoking" is inappropriate; OSHA fails to discuss relevant available data on reported workplace ETS exposures in the workplace.**

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- OSHA states [in Section II.C.6.(b)] that there are "at least 32" epidemiologic studies relevant to a discussion of ETS and lung cancer. OSHA fails to note that the approximately 35 studies publicly available primarily deal with household exposure, assessed most commonly as "spousal smoking." Fourteen studies provide data on reported workplace exposures, which are directly relevant to OSHA's jurisdiction; however, OSHA fails to discuss the workplace data in their entirety.

* * * * * *

- **Taken as a whole, the data on ETS exposures in the workplace do not support a conclusion of increased lung cancer risk.**

- As OSHA's jurisdiction is the workplace, not the home, the spousal smoking data are not the "best available data" for OSHA to use in promulgating its Proposed Rule. While OSHA erroneously characterizes the spousal smoking studies as studies of "nonsmoking housewives" [59 FR 15993], not all the women included in the studies were "housewives"; in fact, a number of the studies cited by OSHA report estimates of lung cancer risk for workplace ETS exposure. [Exs. 8-36, 8-47, 8-106, 8-119, 8-164, 8-171, 8-192, 8-283, 8-292, 8-326] Additional workplace data are found in studies not referenced by OSHA.

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- The availability of risk estimates for workplace exposure was pointed out to OSHA in Philip Morris' submission to Docket H-122 in response to OSHA's Request for Information on Indoor Air [Ex. 3-1074, response to question 2(a)iii)], and in a number of other submissions to Docket H-122 [e.g., Exs. 3-331, 3-1067, 3-1073].

- Of the 14 epidemiologic studies on spousal smoking which include an estimate of workplace ETS exposure, nine were performed in the United States, two in European countries and three in Asian countries.

- In a study published in 1992, Brownson and colleagues reported on data from a case-control study of Missouri women who were lifetime nonsmokers or former smokers. [Ex. 8-36]

- This study is notable for its large sample size, as over 600 lung cancer cases were enrolled, more than 400 of whom were self-reported lifetime nonsmokers. The authors wrote:

> In general, there was no elevated lung cancer risk associated with passive smoke exposure in the workplace (not shown in table). Only lifetime nonsmokers showed a slight increase in risk at the highest quartile of workplace exposure (OR = 1.2; 95% CI = 0.9, 1.7).

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- As the above paragraph indicates, these authors failed to present their overall risk estimate for workplace smoking, which was apparently not statistically significant. The risk estimate that was presented, that is, the one for the most extreme self-reported exposure category, was also not statistically significant.

- Another U.S. study is the 1988 Ph.D. dissertation of Butler. [Ex. 8-47] This cohort study followed two groups of California Seventh-Day Adventists, members of a religious sect who adhere to certain lifestyle choices, e.g., abstinence from smoking, caffeine and red meat. Despite the lifestyle differences suggested by membership in this sect, Butler's data have been included in discussions of workplace ETS exposure. For males, Butler reported a risk estimate of 1.72 (95% CI 0.33-9.04); for females, the reported risk estimate was 1.47 (95% CI 0.15-14.06), for having worked with a smoker for eleven or more years. Despite the large number of individuals enrolled in the study, very few lung cancer cases were obtained, and the resulting extremely small sample size is a major flaw in this study.

- Another American study was first published in 1991 by Fontham and colleagues. [Ex. 8-106] It represented a preliminary report on a case-control study of women in five U.S. cities,

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and is extensively relied upon in OSHA's Proposed Rule. For all lung cancer cell types combined, an odds ratio of 1.34 (95% CI 1.03-1.73) was reported for those women who reported that they were ever exposed to ETS in an occupational setting. Fontham and colleagues (1994) have recently published a report on all five years of the study. They present a "crude" risk estimate for workplace exposure of 1.12 (95% CI 0.91-1.36), which changes dramatically after adjustment for a number of variables to 1.39 (95% CI 1.11-1.74). The magnitude of the change following adjustment is much more pronounced for the workplace risk estimate than for the other risk estimates in the paper. Fontham and colleagues do not address this apparent discrepancy. Because of OSHA's reliance on the 1991 Fontham, et al., study, it is presumed that the second study will be used by OSHA as the rulemaking proceeds.

- Another U.S. study, by Garfinkel and colleagues, was a case-control study of hospitalized women in New Jersey and Ohio, published in 1985. (Ex. 8-119) It included the following estimation of workplace exposure to ETS:

> The interviewer also asked about the average number of hours a day the woman had been exposed to the smoke of others at any time during the past five years, during the past 25 years at home, while at work . . .

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- The authors reported the following:

> [The] OR for exposure at work during the last five years was 0.88 [95% CI 0.66-1.18; 14 cases, 52 controls]; for the last 25 years, it was 0.93 [95% CI 0.73-1.18; 34 cases, 118 controls].

- These two point estimates represent negative associations between reported ETS exposures in the workplace and lung cancer in nonsmokers.

- Conclusions based on a case-control study of 191 men and women in New York State were reported in 1990 by Janerich and colleagues [Ex. 8-164], who wrote:

> Exposure in the workplace was measured by recording the number of smokers who worked with each study subject during his or her lifetime and the amount of time the subjects spent working with these smokers. These exposures were compared for case patients and control subjects. Estimating the odds ratio as a continuous variable for an equivalent differential of 150 person-years of exposure gave an odds ratio of 0.91 (95 percent confidence interval, 0.80 to 1.04), indicating no evidence of adverse effect of environmental tobacco smoke in the workplace. [Emphasis added]

- In 1984, Kabat and Wynder published results of a case-control study of hospitalized individuals, mostly from New York City.

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[Ex. 8-171] A total of 25 male cases and 53 female cases and their matched controls were included.

- The authors wrote:

> The plausibility of a role of passive inhalation in lung cancer can be questioned on several grounds . . .
>
> Cases do not differ from controls except for the greater exposure to cigarette smoke at work reported by male cases compared to male controls.

- The authors reported that 18 of 25 male cases versus 11 of 25 controls reported being exposed to ETS in the workplace. This result was statistically significant at P = 0.05. The point estimate for workplace exposure of males was reported elsewhere as 3.27 (95% CI 1.01-10.6).

- However, the authors' reported data for women are inconsistent with their conclusions on men; 26 of 53 female cases versus 31 of 53 controls (i.e., fewer cases than controls) reported exposure in the workplace. This result, a point estimate of 0.68 (95% CI 0.32-1.47), is not statistically significant.

- In 1990, Kabat reported preliminary data from an American Health Foundation case-control study, which then included 90

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cases and 247 controls. Kabat reported that "preliminary analyses of the data do not indicate any striking ETS exposure differences between cases and controls." Specifically, he reported odds ratios for men of 0.98 (95% CI 0.46-2.10) and for women of 1.00 (0.49-2.06), for reported workplace exposure.

- One of the European case-control studies to assess workplace exposure was conducted on hospitalized women in Athens, Greece. Based on 89 cases and 118 controls, the authors conclude: "The effect of exposure to passive smoking at work was very small and not statistically significant (the RR between extreme quartiles was 1.08 (0.24-4.87))."

- Koo and colleagues, in their 1987 case-control study of women in Hong Kong, included an assessment of workplace exposure in accounting total lifetime exposure to ETS. [Ex. 8-183] The authors concluded:

> On the basis of our extensive life-history data, we were able to calculate the total years, hours, mean hours/day, and cigarettes/day to which the subjects had been exposed to tobacco smoke at home or at work.
>
> Despite such detailed accounting, we were unable to find a significant trend in the crude or adjusted RR for these 4 lifetime measurements of passive smoking.

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- In a 1984 publication, Koo and colleagues reported a risk estimate for women exposed at the workplace of 0.91; it was reportedly not statistically significant.

- Another European study including an assessment of ETS exposure in the workplace and nonsmoker lung cancer was published in 1986 [Ex. 8-192]. The authors wrote that "overall the results showed no evidence of an effect of passive smoking on lung cancer incidence among lifelong nonsmokers," although they presented no odds ratios for workplace exposure. The following point estimates have been presented by one of the authors of this study in a recent book: for females, 0.63 (95% CI 0.17-2.33) and for males, 1.61 (95% CI 0.39-6.60).

- Shimizu, et al., reported that, in their case-control study of 90 women in Nagoya, Japan [Ex. 8-283]:

> Passive smoke exposure at work was not clearly associated with female lung cancer, although the relative risk was slightly elevated (RR = 1.2).

- That reported relative risk was not statistically significant.

- In 1992, Stockwell and colleagues published data from a case-control study of nonsmoking women in Florida. [Ex. 8-292]

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The authors wrote: "We found no statistically significant increase in risk associated with exposure to environmental tobacco smoke at work." However, they failed to present the data associated with this index of exposure.

- In 1985, Wu and colleagues reported on a case-control study of women in a Los Angeles, California tumor registry. (Ex. 8-326) For adenocarcinoma, the authors wrote, "we did not observe any elevated risk associated with passive smoke exposure . . . at work (RR = 1.3; 95% CI = 0.5-3.3)."

- A joint Chinese-American study of women in Shenyang and Harbin, two industrial cities in northeast China, reported that 228 cases and 301 controls had been exposed to ETS in the workplace. A relative risk of 1.1 (95% CI 0.9-1.6) was calculated, which the authors described as a "small excess risk," although it was not statistically significant. The authors also noted that "there were no significant dose-response trends associated with years of passive smoke exposure at work."

- **While the same criticisms that apply to the spousal smoking risk estimates apply to the workplace risk estimates (no actual measurements of exposure, failure to account for sources of bias and for potential confounding factors, poor**

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study design, weak reported associations), the workplace data are, nevertheless, most appropriate for OSHA's purpose.

- Only two of the reported risk estimates are statistically significant. The overwhelming majority, 16 of 18 risk estimates, are not statistically significant. **Taken as a whole, these data do not support the existence of an association between workplace exposure to ETS and lung cancer risk in nonsmokers.**

* * * * * *

- **Analyses of the workplace data as a whole, which were not considered by OSHA, do not support the claim of an increased risk of lung cancer due to ETS exposure in the workplace.**

- As EPA did in its Risk Assessment on ETS, to justify extrapolating from spousal smoking to other exposures, OSHA makes the claim at [59 FR 15994] that:

> [H]ealth effects observed and the risk estimates calculated from studies of the general population, or of selected subgroups, such as nonsmoking wives of smoking husbands, are relevant to the working nonsmoking population.

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OSHA continues:

> [R]isk estimates based on residential exposures are expected to accurately reflect occupational risks in most workplaces and possibly underestimate the risk in some workplaces.

- By neglecting the data on ETS exposures in the workplace available in the studies of spousal smoking and lung cancer, OSHA overlooks a serious inconsistency in these data, as did EPA. As recently noted by LeVois and Layard:

> The EPA's fourth point, that ETS exposure in workplaces is comparable to home exposure, and therefore if home exposure can cause lung cancer, so can workplace exposure, is not an argument for dismissing the workplace epidemiology at all. Rather, it simply avoids the question of why, if domestic and workplace exposures are comparable, the combined workplace data do not indicate any ETS-lung cancer association.

- LeVois and Layard conclude:

> The fact that workplace studies produce a risk estimate that disagrees with the estimate derived from aggregated spousal smoking studies cannot be dismissed by making speculative assumptions about study design validity. . . . The workplace ETS study design avoids problems of spousal concordance with respect to lung cancer risk factors and introduces fewer potential biases and confounders than are present in the spousal

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study design. Thus, workplace ETS-lung cancer data are probably <u>less</u> flawed than are the spousal smoking data. [Authors' emphasis]

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- **OSHA should utilize all the available data on workplace ETS exposures from the epidemiologic studies on ETS and lung cancer.**

- In its Proposed Rule, OSHA arbitrarily chose the workplace smoking risk estimate from the Fontham, et al., (1991) study to use in its calculation of risk. [Ex. 8-106] As detailed above, the reported result of Fontham, et al., both in the 1991 report and the 1994 report, is one of only two statistically significant risk estimates for workplace exposure. OSHA fails to address what would have happened to its calculations of risk if the risk estimate from another of the workplace studies, such as that of Janerich, et al., were used instead.

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- **OSHA's calculation of attributable risk is based on a single, arbitrarily selected risk estimate; it would seem to be highly**

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sensitive to changes in the values of the variables used; OSHA fails to discuss the uncertainty of this estimate.

- The choice of the risk estimate from the Fontham, et al., 1991 study [Ex. 8-106], which OSHA attempts to justify [Section IV.D. (59 FR 15995)] on the basis of the quality of the study, nevertheless seems arbitrary, given the amount of additional workplace data available.

- **OSHA arbitrarily ignores 13 other studies that give workplace risk estimates, and arbitrarily switches from reliance on the spousal smoking data in the rest of its text, to a workplace estimate for the attributable risk calculations.**

* * * * * *

- **The Fontham, et al., 1994 study, though based on a large sample of nonsmoking women, can be criticized.**

- If OSHA, as anticipated, relies on data from the second report on the Fontham study to replace the data from the interim report cited in the Proposed Rule, it is submitted that OSHA should do so carefully. The makeup of this study population is likely quite dissimilar to the United States workforce as a whole.

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- OSHA has available data from 14 worldwide workplace studies or nine United States workplace studies, including data on both men and women. Rather than arbitrarily choosing one study, which, despite its claimed methodological advances, still does not resolve the issues of accurate exposure assessment or misclassification of smokers as nonsmokers, OSHA should consider all the available data on workplace exposures to ETS.

- The following are illustrative comments regarding the 1994 Fontham, et al., report:

(1) Despite the study's use of cotinine to assess current tobacco use, the authors acknowledge that misclassification of ever smokers as lifetime never smokers is "problematic" because there is "no biomarker of lifetime tobacco use." Moreover, only slightly more than half (54%) of cases had cotinine determinations. Thus, recent active smoking was not even excluded for nearly half of the cases.

(2) While the authors stress that their study is a multicenter case-control study, if the characteristics of the study population are examined, it is seen that the vast majority of cases and controls come from two areas in California (Los Angeles and the San Francisco Bay area). Yet, the authors do not indicate that air pollution, which has been

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suggested to be a lung cancer risk factor, was "adjusted" for in their analyses. In fact, the authors provide no breakdown of the data by study center, and it is not possible to ascertain whether the reported risks were consistent across the centers. Heterogeneity in the data among study sites would argue against combining the data as was done in this paper.

(3) Other potential confounders that were not considered in the analyses are dietary saturated fat intake, recently reported by Alavanja, et al., to be associated with relative risks of lung cancer as high as 6.0 to 11.0. The risk was highest in nonsmoking women with adenocarcinoma; over 75% of the cases in the Fontham, et al., study were adenocarcinomas. Alcohol consumption, another potential confounder, was also not mentioned. Recent studies have reported that smokers, and the persons living in their households, are likely to consume more fatty foods and more alcohol.

(4) The presentation in the Fontham, et al., study does not provide data for the possible associations between diet and other potential confounders and lung cancer. It is thus impossible to judge whether fruit and vegetable consumption was associated with lung cancer risk but not with smoking status, or with smoking status but not with lung cancer risk.

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The reader must take the authors' position that the factors were not confounders at face value, without the opportunity to examine the data.

(5) The "adjustment" of the reported risk estimates is difficult to interpret, as the adjustments take into account both study design variables (e.g., subject age) and potential confounders. It is not possible to determine what might be affecting the adjustment. In particular, the dramatic upward shift (1.12 to 1.39) in the risk estimate for workplace exposure is puzzling and surprising. The shift is opposite the direction expected, and is of a magnitude unlike the other adjustments in the paper.

(6) The study population characteristics also reveal that over 70% of cases and controls were aged 60 or older. This calls into question the accuracy of childhood exposure estimates provided by these women, who were asked to recall parental smoking habits of more than 50 years ago.

(7) The socioeconomic and educational composition of the study population argues against generalizing results reported from this study to the United States population as a whole. The majority of cases and controls were drawn from low socioeconomic strata: more than 40% had household incomes of

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less than $20,000. In terms of education, one-third of cases had no more than a high school education.

(8) The conclusion stated in the abstract of the paper -- "Exposure to ETS during adult life increases risk of lung cancer in lifetime nonsmokers" -- gives the appearance that the reported results are applicable to both men and women, when in fact, only women were studied.

(9) Fontham and colleagues neglect to discuss the available workplace data from other spousal smoking studies. Of particular interest is the note that several large recent case-control studies (Janerich, et al.; Brownson, et al.; Stockwell, et al.; Wu-Williams, et al.) have reported results for workplace exposure that were <u>not</u> statistically significant. Fontham, et al., should have put their data in context.

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- **OSHA fails to reference the numerous criticisms that have been made concerning the epidemiologic studies of reported ETS exposure and lung cancer**

- OSHA does not address the issue that actual ETS exposures were not measured in any of these studies reporting data on workplace exposure or spousal smoking.

- These studies relied upon questionnaires to provide an estimate of exposure, usually presented as the smoking habit of the cases' husbands.

- Concerns about the reliability of questionnaires used in ETS studies have been raised in the scientific literature.

- Based on the text of the Proposed Rule, OSHA does not appear to be aware that members of the scientific community have criticized the epidemiologic studies on ETS exposure and lung cancer for failing to consider certain factors, namely bias and confounding, that could affect the validity of the studies' risk estimates.

- The impact of such factors is particularly important in studies that, like these studies, report risk estimates that are "weak." A weak association is represented by a risk

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estimate of less than 2.0 or perhaps even less than 3.0. As Wynder notes:

> [E]pidemiology has problems when the associations are of a low order of magnitude. In such instances, findings in the literature are, in general, inconsistent. . . .
>
> When risks are small, and especially when effects occur many years after their causes, detecting them, estimating their magnitude, and assessing their importance for the community in light of other relevant factors pose problems of study design, data collection, analysis, and interpretation which can be exceedingly difficult. (p. 139)

- A detailed discussion of criticisms relevant to evaluation of the spousal smoking studies may be found in the Philip Morris submission to OSHA's Request for Information on Indoor Air. [Ex. 3-1074, Question 2(a)iii] Other submissions discussing the limitations of these studies include Exs. 3-331 and 3-1195.

- In the Proposed Rule, OSHA simply writes, without referencing its contentions, that:

> Many potential sources of bias, such as publication bias (the tendency of scientific journals to publish studies with positive results), misclassification bias (smokers or former smokers claiming to be nonsmokers), and recall bias (the reliance on self-reporting of personal smoking habits and exposure to

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others' tobacco smoke) can not account for the elevation in risks seen in these various studies.

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- **OSHA, like EPA, has the erroneous impression that a single confounder must apply to all the studies in order for it to be important.**

- Despite OSHA's claim to the contrary, the very diversity of the spousal smoking studies makes it exceptionally difficult to compare them in any meaningful way. It is not logical, given this diversity, to expect that the same lifestyle variables would pertain to a population in China as to a population in Sweden or the United States. **A confounder need not be common to all the studies.**

- In epidemiology, a confounding factor must meet one condition: it must be associated both with the exposure variable being investigated (here, spousal smoking), and with the endpoint under consideration (here, lung cancer). As noted in a recent review:

> Because the relative risks or odds ratios for human diseases reported to be associated with ETS exposure are typically no larger than the

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risks for confounding lifestyle factors, epidemiological studies of the association between ETS exposure and chronic disease should be designed to maximize data quality and statistical power.

The ETS and chronic disease epidemiology studies conducted to date have not adequately controlled for all of the known confounding variables.

- Another 1992 review addressed the possibility that confounding factors may have a combined effect on estimations of lung cancer risk.

In the absence of calculations of lung cancer risk when multiple factors apply, one can only speculate on the combined effect on an individual who, for example, might have a family history of lung cancer (RR = 2-4), lived in an urban area (RR = 1.2-2.8), worked in an occupation associated with elevated lung cancer risk (RR = 2 or more), was among the physically less active groups of the population (RR = 2) and, if a female, had the risk associated with a short menstrual cycle (RR = 2.2).

- While these factors may not truly be confounders (that is, associated both with spousal smoking and with lung cancer), but instead, independent lung cancer risk factors (associated only with lung cancer), their potential contributions to lung cancer risk have not been adequately assessed in the spousal smoking studies.

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- Subsequent to the Philip Morris submission to OSHA's RFI, new studies have been published that provide additional relevant data on potential confounders of the claimed ETS-lung cancer relationship, in particular, the possible effects of diet.

- Recent studies indicate that the diet of nonsmokers is related to the presence or absence of smokers in the household. The studies report that nonsmokers who live in smoking households "have a diet more like smokers," consisting of more fried and fatty foods, more alcohol, and less fresh fruits and vegetables.

- Some authors suggest that differences in lifestyle, such as diet, may influence differences in disease risk reported when smoking and nonsmoking households are compared.

- For instance, a 1992 British study examined the consumption of fried foods, fats, fruits, vegetables, and sweets in smokers, nonsmokers, and exsmokers. The authors reported that nonsmokers who live in smoking households "have a diet more like smokers," and that "diet could be an important confound in epidemiological studies of ETS." The authors also noted:

> Our analysis showed that non-smokers in smoking households ate fried food more often, more chips [french fries], less fruit in

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winter, more butter and less margarine high in polyunsaturates than non-smokers in non-smoking households. As we have pointed out, these habits are thought to increase the probability of cancer.

These results suggest that it is wise to show caution when interpreting the disease patterns of non-smokers in smoking households. Studies to date have failed to take into account the effect that differences in dietary and lifestyle behaviour between 'smoking' households and 'non-smoking' households may have on the incidence of cancer or heart disease.

- In a 1993 paper, the same authors reported that, in addition to having higher intakes of saturated fats, never smokers living in smoking households consumed fats more often, drank more alcohol, and ate fewer root vegetables and cereal than did never smokers living in nonsmoking households.

- A large study conducted in the U.S. recently reported that nonsmoking women who consumed large amounts of saturated fat (i.e., a kind of fat found in meats, butter, and lard) had strongly elevated risks for lung cancer. Although the authors did not compare their data on fat intake to household smoking status, they did note that "passive smoking did not affect risk estimates" in their study. The risk of lung cancer among nonsmokers who reported high consumption of saturated fats was almost three times higher than any overall risk estimate reported in the 35 spousal smoking studies. Indeed, the risks

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reported in the study for lower levels of estimated saturated fat consumption are comparable to any of the overall risk estimates reported in the studies on spousal smoking.

- Another recent U.S. study reported that higher intake of raw fruits and vegetables, vitamin E supplements, and dietary beta carotene (a precursor of vitamin A) is associated with a statistically significant reduction in nonsmoker lung cancer risk.

- If, as other data suggest, smokers and the persons who live with them are likely to consume less of these food items, then those individuals might have an increased risk of lung cancer. Whole milk intake was also greater among lung cancer cases in this study, which the authors suggested possibly "reflects an effect of dietary fat."

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- **OSHA'S treatment of the spousal smoking data is not only inappropriate, but inaccurate and incomplete.**

- Regardless of the fact that OSHA's reliance on the spousal smoking data in much of the Proposed Rule is inappropriate, OSHA should be aware that its treatment of the spousal smoking

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data is nonetheless inaccurate and incomplete. Inclusion of all available spousal smoking studies is important because these very studies contain the workplace data relevant to OSHA's jurisdiction.

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- **OSHA's list of spousal smoking studies is incomplete and inaccurate; OSHA has failed to consider all available data.**

- In addition to the 27 spousal smoking studies referenced by OSHA, there are a number of spousal smoking studies that were not included in OSHA's Proposed Rule.

- One of the studies that OSHA failed to consider, Wu-Williáms, et al., was conducted in China and is one of the largest case-control studies on this issue published to date. Wu-Williams and colleagues report, for spousal smoking, a statistically significantly negative risk estimate.

- Another of these studies, Kabat (1990), is a preliminary report on a United States case-control study. That initial report, which presented no statistically significant risk estimates, suggests that this study is controlling for a number of potential study design problems.

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- OSHA's citations of lung cancer studies at 59 FR 15980 are inconsistent when compared to the studies cited in Table IV-1. [59 FR 15993]

- OSHA "double-cites" at least one study, by treating Gillis, et al., [Ex. 8-122] and Hole, et al. [Ex. 8-148] as unique studies. These two papers are both reports from the same Scottish cohort study. By treating them as two separate studies, OSHA essentially counts the data twice.

- Two of the papers cited by OSHA have been rejected in other reviews of the literature on ETS and lung cancer. The reasons for those rejections are described below:

(1) Katada, et al., 1988 [Ex. 8-175]: The reference categories (i.e., nonexposed women) are too small to allow appropriate calculations of relative risk (because all of the cases reported ETS exposure). The U.S. EPA did not use the study in any of its analyses. [Ex. 8-311]

(2) Sandler, et al., 1985 [Exs. 8-275 and 8-276]: The methodology and interpretation of this study has been criticized in the scientific literature (e.g., one scientist described Sandler's work as "seriously flawed"). The data presented are of limited value; for instance, the lung cancer

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estimates are based on only two cases. Neither the U.S. EPA (1992) [Ex. 8-311] nor the National Academy of Sciences (1986) [Ex. 8-239] included this study in their summary analyses of ETS issues.

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- **OSHA's argument in support of the case-control studies on spousal smoking is flawed and reveals a lack of familiarity with the available literature.**

- At 59 FR 15980, OSHA states:

> [T]he relative risks that were estimated from prospective study data are similar to those estimated from case/control [sic] study data. Biases that may be problematic in case-control studies are not a problem in prospective studies. Since the results from both types of studies are similar it is apparent that these biases are not important in the case-control studies (e.g., misclassification bias and recall bias). This information strengthens the confidence of a causal connection.

- OSHA fails to provide references to support the contention that biases are not a problem in cohort studies, nor does OSHA provide references to justify its conclusion that biases are not operating in the case-control studies.

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- Misclassification of smoking status can certainly occur in a cohort study, just as in a case-control study. For instance, a person may misreport his or her smoking status in the initial interview; personal smoking status may change over the course of the study; spousal smoking status may change over the course of the study. Follow-up in cohort studies must take these possibilities into account. Similarly, confounding factors associated with marriage to a smoker could operate in a cohort study as well as in a case-control study.

- While the cohort study may well be a preferred tool for epidemiologic research, OSHA has failed to recognize that the cohort studies on spousal smoking published to date have been criticized in the scientific literature.

- Of the four such studies available, two [Gillis/Hole, Exs. 8-122 and 8-148, and Butler, Ex. 8-47], have less than ten nonsmoker lung cancer cases each. These extremely small sample sizes reduce confidence in the risk estimates reported in those studies.

- The other two studies, Hirayama [Exs. 8-142 and 8-143] and Garfinkel [Ex. 8-118], report data on larger numbers of nonsmoking women. The results of the two studies, however, are not consistent, with Hirayama reporting a statistically

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significantly overall risk estimate, while Garfinkel reported no statistically significant overall risk for spousal smoking.

- The Hirayama study has been heavily criticized in the scientific literature, for its mathematical errors, unconventional statistical methods, and inconsistencies in the data presented. In particular, researchers have criticized Hirayama's techniques of age adjustment, an important consideration since age may act as a confounding factor in epidemiologic calculations.

- It has been noted that Hirayama did not divide his study population into appropriate age groups, and that he also adjusted his analyses by husband's age, rather than by wife's age, contrary to common epidemiologic practice. Information available about the study also suggests that as few as 12% of the cases were histologically confirmed. This means that bias could have been introduced if, among the 88% not confirmed, some died of causes other than lung cancer.

- Thus, had OSHA critically examined the cohort studies of spousal smoking and lung cancer, and reviewed relevant literature critical of those studies, it would have seen that the cohort studies are not free of problems, contrary to its unsubstantiated claims.

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- **OSHA fails to provide sufficient information to justify its classification of the spousal smoking studies in support of its quantitative risk assessment.**

- At 59 FR 15992, OSHA states:

> As a first step in this risk assessment, OSHA critically reviewed epidemiologic studies associating exposure to ETS . . . with adverse health effects. The purpose of such a critical evaluation was to determine whether exposure to ETS is a causal factor in cancer . . . [59 FR 15992]

- However, OSHA fails to provide adequate information for the reader of the proposal to evaluate how OSHA conducted this "critical evaluation" or review.

- **OSHA's evaluation focuses on the data on spousal smoking. These are not the best available data for OSHA's purpose, as other data exist on ETS exposures <u>in the workplace</u> and lung cancer risk.**

- In its discussion, OSHA continues [59 FR 15992-15993]:

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> OSHA evaluated studies on exposure to ETS to determine the importance and weight of each study in the overall hazard identification process. Of those, it was determined that fourteen showed a statistically strong association between exposure to ETS and lung cancer . . . Studies that were determined to be positive by OSHA's review standards met standard epidemiologic and statistical criteria to support causation. [59 FR 15992-15993]

- OSHA's Proposed Rule does not describe in sufficient detail the criteria used to determine that certain of the spousal smoking studies on lung cancer were "positive," "equivocal with a positive trend," and "equivocal." Although OSHA lists the studies according to these categories in Table IV-1 [59 FR 15993], that table does not include any numerical data.

- It is not possible to determine whether OSHA used a single risk estimate from the study (and if so, which one), or whether OSHA somehow evaluated all the data presented in each study.

- Without the criteria used by OSHA, the classification gives the appearance of being arbitrary and based on unknown subjective standards.

- In particular, it is not clear how OSHA can make this statement given the lack of statistical significance in the

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spousal smoking studies (only six report statistically significant overall relative risks), and specifically, the statistically nonsignificant overall risk estimates included among the 14 studies in OSHA Table IV-1 that are described as "positive for an association" [59 FR 15980], "positive" [59 FR 15993], or "statistically strong" [59 FR 15992]. Of those 14 studies, less than half report statistically significant overall risk estimates.

- If the overall risk estimates reported in these studies are examined according to the criteria of statistical significance and the magnitude of the reported risk estimates, a different classification emerges.

- Of 35 currently available studies, 11 report overall risk estimates less than or equal to 1.0; one of these is statistically significantly negative.

- These risk estimates are compatible with the hypothesis that there is no increased risk associated with ETS exposure, reported as spousal smoking.

- Furthermore, 17 of the studies report overall risk estimates ranging from 1.0 to slightly greater than 2.0, none of which is statistically significant. Therefore, all of these risk

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estimates are compatible with the hypothesis of no association.

- Only seven studies report overall risk estimates that are statistically significant. **In summary, then, 28 of 35 spousal smoking studies (80%) report overall risk estimates that do not support a conclusion of increased risk.**

- **It is particularly puzzling how OSHA can justify its description of the Brownson, et al., 1992 study's reported results as "positive" when that study reports an overall risk estimate of 1.0. According to epidemiologic convention, 1.0 is the "no-effect" level.**

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- **OSHA's choice of "summary analyses" is restricted to meta-analyses of spousal smoking data rather than the more appropriate workplace data.**

- OSHA's Table IV-3 is "Published Risk Estimates for Lung Cancer." The numbers in the table are all summary risk estimates calculated by combining risk estimates from a number of epidemiologic studies, through a procedure called meta-analysis.

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- This is not made clear in the Notice; in fact, only one of the risk estimates in the table is identified as based on "pooled studies." [Ex. 8-311] Moreover, the summary risk estimates presented by OSHA are based on the spousal smoking data, rather than the data on workplace ETS exposures that have been published.

- Setting aside the question of the appropriateness of using meta-analysis to combine data from epidemiologic studies, if OSHA references meta-analyses, then their list should be accurate and complete. Table IV-3 is neither.

- For instance, OSHA fails to indicate the number of studies included in each meta-analysis, and whether the analyses are restricted to a certain set of studies. The meta-analyses are not completely comparable, as they incorporate different subsets of the universe of available studies.

- A review of more recent meta-analyses reveals that the summary risk estimates are sensitive to the inclusion or exclusion of studies.

- The example most illustrative of this is provided by the meta-analysis from the 1992 EPA Risk Assessment on ETS. [Ex. 8-311] EPA reported a summary risk estimate of 1.19 (90% CI

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1.04-1.35) based on 11 spousal smoking studies conducted in the United States. In a recent paper, LeVois and Layard report:

> Using the EPA's methods and assumptions, we have calculated a summary relative risk of 1.07 from a meta-analysis of 13 U.S. female spousal smoking studies, including these two recent studies [Brownson, et al., Ex. 8-36, and Stockwell, et al., Ex. 8-292]. This relative risk, with 95% confidence interval of 0.95-1.21, is not statistically significant.

- Thus, the inclusion of two additional studies in the meta-analysis effectively reverses the conclusion of the EPA Risk Assessment on ETS. **The summary relative risk is no longer statistically significant, and, therefore, does not support a conclusion of an association between spousal smoking and lung cancer.**

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- **OSHA'S claim that animal inhalation studies support the "carcinogenicity" of ETS is not supported by the scientific literature.**

- At 59 FR 15980, OSHA proposes: "Animal studies have shown the carcinogenicity of cigarette smoke." This assertion, which OSHA fails to reference, is directly in contrast to a recent review of the relevant literature by Rodgman, who cautions:

> Classifying a substance as tumorigenic or 'carcinogenic' can be misleading. Often, these terms are overinterpreted. One must be aware of the precise meaning and limitations of the terms tumorigenicity and carcinogenicity when applied to specific compounds and must exercise considerable care in the use of these and related terms.
>
> Many of these 43 MS and/or tobacco components [claimed to be carcinogens] should be excluded from the list on the basis of published data on their tumorigenicity (or lack of it) in laboratory animals at levels determined in MS, their lack of tumorigenicity in most instances on inhalation, and the equivocal evidence of their tumorigenicity in humans at levels in MS.

- In this major review, Rodgman also writes:

> [I]nhalation studies from 1936 to date involving lifetime exposure of laboratory animals to whole cigarette MS have consistently failed to induce squamous cell carcinoma . . .

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> The failure to produce in MS-exposed laboratory animals the tumor type reported to be associated with smoking in humans is important not only with regards to the biological properties of MS itself but also with respect to that of diluted MS delivered to the caged animals. . . .
>
> If, as Stewart and Herrold (1962) noted, these smoke-inhalation experiments more closely resembled passive smoke (or ETS) exposure than human exposure during actual smoking, then substantial evidence is available to demonstrate that exposure to 'passive smoke' (or ETS), more concentrated than that encountered in the human situation, is ineffective in induction of the tumor type supposedly associated with cigarette smoking in humans . . .

- These conclusions undermine OSHA's contention, and make further discussion of the literature cited by OSHA of limited value.

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- **OSHA's discussion of animal studies suggests a failure to understand the literature, and misrepresents the conclusions of a number of papers.**

- **OSHA's discussion of experimental animal data in the Proposed Rule represents a selective, biased review of the data. The presentation of data on animal exposures is neither balanced nor accurate.**

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- **In addition to misstatements of studies' conclusions, and misrepresentations of studies' data, OSHA's discussion of animal studies is pervaded by the following errors: assuming that mainstream smoke, sidestream smoke, and ETS are equivalent enough to be used interchangeably; and failure to acknowledge the differences among subchronic and chronic inhalation experiments.**

- OSHA introduces its discussion of the animal studies by saying:

> Currently, OSHA is aware of only a few experimental inhalation studies with sidestream smoke or ETS reported in the literature. A discussion of these studies follows. [Emphases added]

- However, OSHA's choice of studies to include shows that OSHA did not restrict its analysis to sidestream or ETS studies. For instance, the first two papers referenced deal with gas-phase smoke.

- Their inclusion implies that OSHA may have made the erroneous assumption that the gas phase of whole smoke is equivalent to sidestream smoke or ETS. If so, this is a distinct misconception; any type of tobacco smoke (mainstream, sidestream, or ETS) consists of both a gas and a particulate

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phase. If the authors of OSHA's Proposed Rule were not operating under this misunderstanding, then they instead misrepresented the articles under discussion.

- Also, OSHA claims that "data suggest that sidestream smoke may contain more carcinogenic activity per milligram of cigarette smoke condensate than does mainstream smoke," citing to Ex. 3-689D. The exhibit available to the public was not labeled in such a way that Part "D" could be identified. This made it difficult to assess the reference for OSHA's claim.

- In discussing Otto and Elmenhorst's paper [Ex. 8-247], OSHA states that this research has "shown that there are carcinogenic constituents in the vapor phase of tobacco smoke." Contrary to OSHA's assertion, the authors write: "the conclusion seems justified that tumor-inducing factors must be in the particle-phase of the smoke" [emphasis added].

- The authors also indicate, in the summary of the study, that their chronic exposure regimen "had no significant effect on the spontaneous tumor-rate." Thus, this study, even given OSHA's misrepresentation of its conclusions, in no way supports OSHA's claim that the "carcinogenicity" of tobacco smoke has been shown in animal experiments.

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- Leuchtenberger and Leuchtenberger [Ex. 8-197] used neither ETS nor sidestream smoke as a surrogate for ETS. According to their paper, they used "whole fresh cigarette smoke" or "its gas phase alone." The Leuchtenberger article is not an chronic inhalation study of ETS or sidestream smoke, as implied in the preceding paragraph. The results cited by OSHA (pulmonary adenomas and adenocarcinomas in male mice) are but one aspect of the data reported in the study.

- The authors comment that those changes could be found in control animals at a later age and lower frequency. The authors note that "chronic inhalation of the gas phase of fresh cigarette smoke did not evoke bronchogenic carcinoma" [emphasis added]; they also indicate that no bronchogenic carcinomas were observed in mice exposed to whole fresh smoke. Thus, the data from this study do not support OSHA's position.

- Harris, et al., [Ex. 8-135] is correctly acknowledged as a mainstream smoke study by OSHA. With regard to their reported results, the authors stated that "spontaneous" tumors appeared in their control animals during the course of their chronic study, and said that "it would no longer be accurate to refer to the inhaled smoke:air mixtures as the cause of these tumors but merely as eliciting a higher incidence." Thus, according to the authors themselves, this study's data do not support a

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determination that cigarette smoke causes lung cancer in experimental animals.

- In Mohr and Reznik [Ex. 8-226], one of the references cited by OSHA to support the statement "Studies have also reported hyperplasia and metaplasia in the trachea and bronchi of mice exposed to cigarette smoke by the inhalation route," the variability of the results reported from smoke inhalation studies is discussed. More importantly, Mohr and Reznik write:

> [T]he majority of investigations in tobacco smoke research have been conducted by some form of inhalation technique. . . . Nevertheless, no researcher has succeeded as yet in producing a significant incidence of pulmonary tumors. (p. 347) [emphasis added]

- Thus, in its selective treatment of these data, OSHA uses a lengthy review paper to support a single statement. However, OSHA fails to discuss the concluding statements made by the authors of that review.

- **Arguably, the most important point in this review paper is what the authors noted above: that animal inhalation studies using tobacco smoke have not reported a significant increase in pulmonary tumors in exposed animals. This statement casts**

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doubt over all of OSHA's contentions that animal inhalation experiments support the claimed "carcinogenicity" of ETS.

- In the discussion of a paper by Davis, et al. [Ex. 8-79], which again deals with chronic exposure to vapor-phase smoke, not sidestream smoke or ETS, OSHA presents the data in such a way that the paper's lack of a statistically significant result is effectively obscured. While OSHA's statement that: "Pulmonary squamous neoplasms were detected in female Wistar rats exposed to a 1:5 smoke-to-air mixture . . ." is not incorrect, it implies that the tumors were found only in exposed animals.

- If one reads the conclusion of the paper cited, the following statement is found:

> The results provide convincing evidence that, under the conditions of the experiment, exposure to VP did not increase the incidence of any kind of neoplasm at any body site. (p. 467) [emphasis added]

- The authors also note that cellular changes in the respiratory tract were no more frequent in exposed rats than in control rats.

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- While OSHA does make an accurate statement (i.e., that neoplasms were produced), its failure to present the complete picture, namely, that neoplasms were reported no more frequently among exposed than unexposed animals, is deceptive and misleading. The data presented in this paper do not support claims that animal inhalation studies show carcinogenic effects of tobacco smoke inhalation.

- Some of the papers cited by OSHA, in this section which focuses on lung cancer, present data on tumors of sites other than the lung. Studies of this sort provide limited information pertinent to the issue at hand, namely, lung cancer. For instance, Dalbey, et al. [Ex. 8-77], reported a large number of benign adenomas or nasal tumors in chronically-exposed rats. Similarly, Dontenwill [Ex. 8-88] actually commented on the "very rare appearance of lung carcinomas" in his chronic inhalation study of hamsters (only 1 case).

- Bernfeld, et al. [Ex. 8-30] reported on laryngeal changes, not changes to the lungs or bronchi. Moreover, the authors indicated that responses to chronic smoke inhalation varied greatly between the two hamster strains tested. If, then, two strains of the same species can exhibit markedly different responses in an experiment, by combining strains and species

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in the discussion and not considering the unique biology of the different animals tested, OSHA displays a overly simplistic view of biology.

- In the discussion of the Auerbach, et al. [Ex. 8-19] study, in which dogs smoked through a tracheostomy, that is, a tube inserted into a hole cut into the animal's trachea (windpipe), OSHA did not even note that the Auerbach study used the tracheostomy method, as opposed to the exposure chambers used in the majority of the other studies discussed. More importantly, OSHA did not address the appropriateness of this route of exposure to either active smoking or ETS.

- The Mohr and Reznik review [Ex. 8-226], cited by OSHA and discussed here previously, contains the following statements about the use of the tracheostomy method:

> [M]ost importantly, smoking through a tracheostomy is a highly artificial system and bears little resemblance to human experience. This is particularly the case when it is remembered that the normal dilution of smoke air is not achieved by this technique, with the result that the concentration of smoke is much higher than if taken in through the mouth.
>
> The most positive results have been obtained by means of tracheostomies in dogs. However, once again the extreme artificiality of this system prevents any real correlation of the obtained experimental results to humans. (p. 347) [emphases added]

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- Mohr and Reznik are discussing the relevance of data obtained in tracheostomy data to active smoking in humans. The relevance of these data to OSHA's Proposed Rule is certainly questionable, particularly given the extreme dilution of ETS once it is in room air.

- Studies such as Grimmer, et al. [Ex. 8-127], discuss direct pulmonary implantation, in which a beeswax solution, containing a substance to be tested (here, condensed particles and semivolatiles from sidestream smoke), is injected into the animal's lungs. **The relevance of this experimental route of exposure in comparison to inhalation exposure is unclear.** Moreover, the authors of the paper fail to present analyses of the statistical significance of their reported results. It is thus not possible to evaluate whether the paper supports OSHA's claims.

- Dagle, et al., [Ex. 8-75] and Stanton, et al., [Ex. 8-289] report on the injection of a pellet of beeswax containing cigarette smoke condensate into the lungs of rats. Theoretically, this pellet would approximate chronic exposure, as substances "leach" from the pellet over time. However, as the authors of Ex. 8-289 note: "A major disadvantage is the unnatural exposure of respiratory epithelium to the

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carcinogen." Also, both these studies report simply on the development of this technique for bioassays.

- In the subchronic study of Coggins, et al. [Ex. 8-59], aged and diluted sidestream smoke was used as a surrogate for ETS. This substance may be a more appropriate approximation of ETS than are other forms of tobacco smoke.

- While OSHA provides a factual summary of the conclusions of this study, they fail to note that effects (hyperplasia and inflammation) were reported only in animals exposed to particle concentrations some 100 times higher than typical real-world concentrations. Coggins, et al. [Ex. 8-60] also report the same minor, completely reversible histopathological changes. The changes did not progress over longer periods of exposure, and once again occurred only at particle concentrations some 100-fold higher than real-world levels.

- In a 14-day inhalation study, one would not expect lung tumors to develop. Thus, the relevance of the work of Coggins, et al., to OSHA's discussion of cancer is limited. Nevertheless, Coggins, et al. show only minor, reversible cellular changes following intense exposure to a surrogate for ETS.

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- At 59 FR 15981, OSHA cites to a book by Wynder and Hoffmann [Ex. 8-327] (the citation is unclear, particularly with respect to page numbers, as it is not a chapter or even a definable section), discussing "skin-painting" studies in which tobacco tar condensates were applied to mouse skin. In the very book cited, the authors write:

> The bioassay[s] for tobacco products on mouse epidermis have not answered questions on the problem of respiratory carcinogenesis. (p. 145)

- **The relevance of mentioning skin-painting studies in this context is unclear.**

- Reif, et al. [Ex. 8-259] reports on a "case-control" study in which owners of dogs that had died of lung cancer were asked about the dogs' exposures to ETS. Risk estimates for the dogs' developing lung cancer were then calculated. The study's authors note:

> The current study suffers from some of the same limitations found in the studies done in humans, i.e., small sample sizes, imprecise risk estimates, and difficulties in measuring exposure. (p. 238)

- The "risk estimates" reported in this study were not statistically significant. Thus, these data in no way support

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the claim of an association between ETS exposure and lung cancer risk.

- Not only do the data cited by OSHA fail to support OSHA's claims, but they represent a troubling approach to science. OSHA's Proposed Rule should be accurate and balanced: the complete data should be presented fairly, whether or not they support OSHA's position.

* * * * * *

- **OSHA's discussion of animal studies omits certain references concerning inhalation studies.**

- Despite the fact that data from subchronic animal inhalation studies are of minimal relevance to the question of whether animal data support claims of the "carcinogenicity" of ETS, OSHA nevertheless chose to include some subchronic studies in its discussion.

- However, OSHA omitted several studies, which, in the interest of completeness, are described below. None of the studies report data supporting any permanent changes following subchronic exposure of animals to sidestream smoke at levels exceeding those encountered in "real-life" situations.

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- **Haley, et al., 1987a, 1987b:** Preliminary reports on this American Health Foundation study, in which hamsters were exposed to mainstream or sidestream smoke 7 days/week for 18 months, are available; apparently, however, no final report has been published. In those reports, the authors note that smoke-exposed animals were living longer than were sham or cage control animals. No additional information was presented.

- **von Meyerinck, et al., 1989:** Rats and hamsters of both sexes were exposed to sidestream smoke at a concentration of 4 mg/m^3 TPM and 25-30 ppm carbon monoxide for 10 hours/day, five days/week for 90 days. The authors noted about their exposure system: "The levels in the exposure chamber were at least 1 and in some instances 2 orders of magnitude higher than reported for smoke-polluted rooms under real-life conditions." (Elsewhere, the authors described these conditions as "unrealistically high.") One hundred animals of each species were exposed, 115 of each species were sham controls, and 100 of each species were room controls. The authors reported minor, completely reversible histopathological changes in the nasal cavity in rats only, and no alterations in any other part of the respiratory tract.

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- **Teredesai and Pruehs, 1994**: Male rats and male hamsters were nose-only exposed to fresh sidestream smoke (FSS) for seven hours/day, seven days/week for 90 days. One group of 20 animals was exposed to FSS with a total particulate matter (TPM) concentration of 2 ug/L, one to FSS with TPM of 6 ug/L, and one served as a sham exposure group. Histopathological changes described as "slight" were reported in the nose and larynx of exposed rats, "mainly in the high FSS concentration group." These changes were reversible following cessation of exposure. The authors noted that "[n]o smoke-exposure-related histopathological changes were observed in trachea and lungs."

* * * * * *

CARDIOVASCULAR DISEASE

- **OSHA has not provided an adequate scientific foundation for its position that ETS exposure in the workplace increases the risk of adverse cardiovascular effects.**

- OSHA argues that research indicates that ETS exposure has a variety of adverse cardiovascular effects, including both acute effects, relating especially to oxygen supply and demand, and chronic effects, such as atherosclerosis and

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increased risk for the development of and death from coronary heart disease.

- **OSHA does not provide adequate support for its claim that ETS in the workplace should be regulated because of an alleged association between ETS exposure and adverse cardiovascular effects.**

- Much of the supporting literature cited by OSHA deals with active smoking, not ETS.

- Other studies, even though they may deal with ETS, are so flawed and limited in scope that they do not provide a sound basis for cardiovascular disease claims.

- **Perhaps most importantly, actual workplace data on ETS and heart disease are scant. Such data as exist do not support an association between workplace ETS exposure and cardiovascular disease.**

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- **OSHA provides inadequate support for its claims about ETS exposure and thrombus formation.**

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- OSHA argues that ETS exposure is involved in the formation of blood clots. [OSHA addresses the issue of thrombus formation in the Proposed Rule at Section II.C.4.(a). (59 FR 15977)] OSHA cites only two laboratory studies to support this claim.

- Both of these studies focused on platelet activity. In one of these, Burghuber, et al. (1986) [Ex. 8-40], examined platelet function in a group of only nine nonsmokers, following a single exposure to high levels of "ETS." The relevance of this artificial, short-term laboratory procedure to actual workplace conditions is highly speculative.

- Furthermore, these authors acknowledged that their test for platelet function in the laboratory may have no relevance to how platelets act in real life. They stated: "However, as with other platelet function tests, we do not know if this **in vitro** procedure accurately reflects platelet function **in vivo**." (p. 37)

- The authors further acknowledged that it was not known whether their research had implications for cardiovascular function in ETS-exposed nonsmokers. They stated: "Further investigation is needed to elucidate whether this finding is important with respect to a possible increased incidence of thromboembolic

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disease among non-smokers passively exposed to cigarette smoke." (p. 37)

- In another laboratory study cited by OSHA on ETS exposure and platelet function, Davis, et al. (1989) [Ex. 8-80], reported that 20 minutes of exposure to ETS increased platelet aggregation and also increased the number of endothelial cell carcasses in the blood.

- However, this was a highly limited study of only 10 male subjects, for which there was no true control condition. More specifically, in their exposure condition, the nonsmokers sat for 20 minutes in a hospital corridor where patients typically smoked. Not only does this constitute an imprecise ETS exposure, but it is not comparable to the control nonexposure condition. In the nonexposure condition, the nonsmokers sat in a laboratory where smoking was not allowed. A hospital corridor and a hospital laboratory are entirely different environments, involving potential confounding factors such as social conditions, noise factors, ventilation factors and a variety of other differences.

- Other than the two laboratory studies, the only other citation with ETS data cited by OSHA was a 1991 report by Dobson, et al. [Ex. 8-85] This epidemiological study, in addition to

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reporting odds ratios for ETS exposure and heart disease, also provided data on fibrinogen concentrations. However, Dobson, et al. repeatedly noted that there was no statistically significant association of fibrinogen concentration with ETS exposure. Moreover, limitations of this study were explicitly acknowledged by the authors, thus making this paper unreliable as a basis for OSHA's claims.

- For example, Dobson, et al. noted that there were "[d]ifferences in the methods of data collection and truthfulness in reporting smoking habits" between their exposed and nonexposed groups and that this might "have lead to bias." (p. 796) The potential effects of confounding factors, especially socioeconomic status, were noted, as well as the lack of statistical power in their study.

- In general, with regard to their epidemiological procedure, which was the basis for both the odds ratio and fibrinogen data, Dobson, et al. stated: "On balance, the effects of bias and confounding could have lead to overestimation of risks due to passive and active smoking." (p. 796)

- Other citations listed in OSHA's review of the thrombus formation issue are not relevant to ETS. Some merely provide background or theoretical information concerning

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cardiovascular disease processes. [E.g., exs. 8-111, 8-272] Others are studies of active smoking, not ETS. [Exs. 8-157, 8-224]

* * * * * *

- **OSHA fails to adequately support its claim that ETS exposure is associated with vascular wall injury.**

- OSHA argues that ETS exposure may harm the endothelial lining of the arterial wall, but provides almost no support for this claim. [OSHA addresses the issue of vascular wall injury in the Proposed Rule at Section II.C.4.(b). (59 FR 15977)] In connection with this claim, OSHA refers to only one citation -- namely, the Davis, et al. (1989) report [Ex. 8-80], which, as noted in the previous section regarding thrombus formation, is a highly limited and flawed study.

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- **OSHA's discussion of possible mechanisms of effect is not adequately supported; some of the cited references are irrelevant to this issue.**

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- OSHA addresses the issue of possible mechanisms of effect primarily in the Proposed Rule at Section II.C.4.(c). [59 FR 15977] Part of OSHA's discussion of risk assessment in Section IV.F.2, which addresses cardiovascular effects in relation to pharmacokinetic modeling, is also germane.

- In Section II.C.4.(c), OSHA argues that there are three mechanisms by which ETS exposure "may place stress on the heart." The first mechanism is by decreasing myocardial oxygen supply. The primary manner in which ETS exposure theoretically might have this effect, as discussed by OSHA, is via formation of carboxyhemoglobin. OSHA cites only study on this issue which actually involved ETS. This was a 1978 report by Aronow. [Ex. 8-13]

- The Aronow study is widely regarded in the scientific literature as being methodologically weak and unsubstantiated. Furthermore, it is important to note that Aronow has been criticized severely for unethical and dishonest scientific practices, to the extent that the government no longer relies on his data.[1]

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1. (Shephard, R., The Risks of Passive Smoking, London, Croom Helm Ltd., 73, 1982.) (Mintz, M., "FDA, Citing Phony Evidence, Bars Drug Tests by Researcher," The Washington Post, March 23, 1983.) (Peterson, C., "EPA Probe Criticizes a Study Used in Air-Quality Standard," The Washington Post, June 7, 1983.)

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- Although OSHA cites several additional reports in the context of discussing oxygen supply and demand [Exs. 8-242, 8-323, 8-324], these are reports on cigarette smokers, not on nonsmokers exposed to ETS.

- The second mechanism for placing "stress on the heart" mentioned by OSHA is that oxygen demand may be increased via nicotine. However, OSHA does not provide any citations demonstrating that there is an association of ETS exposure with myocardial oxygen demand, much less an association with an increased demand specifically as a result of exposure to nicotine in ETS.

- Perhaps there is a theoretical argument, based on claims that nicotine can be a pharmacological stimulant, for speculating that ETS may be associated with increased oxygen demand. Such an argument, however, does not recognize that the amounts of nicotine in ETS are extremely small and of doubtful physiological or cardiovascular relevance.[2]

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2. [See Part II, Point IIB or Section IV of the Philip Morris written submission for examples of literature, ignored or not adequately addressed by OSHA, which relates to the minute levels of ETS, and of ETS constituents, to which nonsmokers might be exposed, and the doubtful cardiovascular significance of such exposure levels.]

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- The third mechanism discussed by OSHA is that ETS exposure may influence the cellular ability of the heart to utilize oxygen for energy production. The only citation on this point provided by OSHA is Ex. 8-123, which OSHA describes as a study demonstrating that healthy subjects became fatigued quicker when exercising in the presence of ETS. However, OSHA's description of Ex. 8-123 is incorrect. Ex. 8-123 is not a study of exercise performance and ETS. It is not even a research report with original data. It is merely a draft of a review paper by Stanton Glantz and William Parmley.

- In one section of their draft manuscript, Glantz and Parmley discuss an exercise study involving healthy subjects and ETS. This 1985 study by McMurray, et al. is elsewhere referenced by OSHA as Ex. 8-217. However, the McMurray, et al. report does not provide direct measurements of cellular oxygen utilization. Thus, it does not bear importantly on the issue for which OSHA cited it.

- An additional heart disease mechanism proposed to be related to ETS is suggested by OSHA in Section IV.F.2., where cardiovascular physiology is discussed in the context of pharmacokinetic modeling of ETS exposure. In Section IV.F.2., in addition to carbon monoxide and nicotine, OSHA proposes

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that polycyclic aromatic hydrocarbons (PAHs) have been associated with cardiovascular effects.

- To support this claim, OSHA cites the draft manuscript by Glantz and Parmley [Ex. 8-123], which presents no original data. It references several reports primarily dealing with injections of massive amounts of PAHs into chickens and pigeons. Given the doses and manner of administration, it is highly questionable whether this type of study has implications for any sort of inhalation exposure related to tobacco smoke, whether active smoking or ETS exposure.

* * * * * *

- **OSHA's discussion of acute heart effects relies heavily on studies of questionable validity and fails to accurately represent the conclusions of some reports.**

- In this section, OSHA argues that ETS exposure has certain acute effects, such as raising CO levels in the blood, increasing heart rate and blood pressure and affecting blood components that may be involved in atherosclerosis. [OSHA addresses the issue of acute heart effects in the Proposed Rule at Section II.C.4.(d). (59 FR 15977-8)]

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- Much of this section duplicates the claims in OSHA's immediately preceding section on "Possible Mechanisms of Effect." OSHA again relies strongly on highly flawed studies, in particular, the 1978 Aronow study [Ex. 8-16, which is the same as Ex. 8-13] and the studies on platelets by Burghuber, et al. [Ex. 8-40] and Davis, et al. [Ex. 8-80].

- One of OSHA's central points in this section is that exposure to ETS results in a significant increase in carboxyhemoglobin. It is odd that, in introducing this topic, OSHA cites the review and conclusions of the National Research Council (1986).

- The NRC report concluded that if background air has little or no carbon monoxide, then even upper estimates of what might be produced from ETS would "have a negligible effect on carboxyhemoglobin levels." (p. 128) Furthermore, the 1986 Surgeon General's Report, in addressing this same issue, concluded as follows: "Thus, small increments of carbon monoxide due to environmental tobacco smoke may be indistinguishable from that due to endogenous and non-tobacco-related sources." (p. 202)

- OSHA also incorrectly describes that data in Guerin, et al. [Ex. 8-129] as indicating that it is common for workplace ETS

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exposure to be associated with significant increases in COHb levels. In point of fact, Ex. 8-129 concludes the opposite, noting that "studies which quantified the percentage COHb in nonsmokers show very little difference in nonsmokers who were or were not exposed to ETS." (p. 160) Elsewhere in Ex. 8-129, a similar conclusion is reached, noting that nearly all CO in indoor environments arises from sources other than ETS.

> CO has been measured repeatedly in rooms where there is adequate ventilation, with and without cigarette smoking. In many cases, the difference in values is small, and is easily masked by either normal variation in the data or the precision of the analytical measurement. Studies which measure the concentration of COHb in both ETS-exposed and non-exposed subjects is consistent with environmental CO measurements, and have demonstrated no consistent significant differences in most indoor environments. The chief difficulty is interferences from other sources of CO, particularly cooking, heating, and vehicle exhaust. One author (Eatough, 1988) states that about 90% of all CO arises from sources other than ETS. (p. 177) [Ex. 8-129]

- Other literature cited by OSHA in this section also does not provide substantial support for, and sometimes is, at best, remotely relevant to OSHA's claims of acute cardiovascular responses to ETS.

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- For example, OSHA cites Ex. 3-38 to support its claim that ETS has acute effects in angina patients. However, Ex. 3-38 consists of materials from the state of Washington, Department of Labor and Industries, relating to a proposed indoor air regulation. It has no apparent relevance to the context in which OSHA cited it. On the same point, OSHA cites Milhorn (1989). [Ex. 8-222] But Milhorn (1989) is not a study of ETS. It is primarily a review of behavioral issues related to nicotine, as they might be relevant to physicians' advice to their patients about smoking.

- On the issue of potential cardiovascular responses in healthy people, OSHA cites Asano, et al. (1985) and McMurray, et al. (1985). [Exs. 8-18 and 8-17] Although these articles report minor changes in certain cardiovascular variables, such as heart rate, it is doubtful whether these have any physiological significance, even assuming that such responses were actually direct responses to ETS, rather than reflective of a psychological reaction to ETS exposure.

- In supporting its claim that ETS exposure has acute effects on blood components, OSHA again cites Burghuber, et al. [Ex. 8-40] and Davis, et al. [Ex. 8-80], which as noted repeatedly above are very weak, especially relative to the scientific weight OSHA is urging them to carry.

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- OSHA claims that effects of ETS exposure "may be additionally aggravated by simultaneous exposure to other compounds." In support, OSHA cites Ex. 3-446, which consists of comments from a government employee's labor union and appears to provide no substantive information on this issue.

- On this same point, OSHA cites a 1988 review by Eriksen, et al. [Ex. 8-99] This is perplexing, since the conclusions in Ex. 8-99 generally track those in the 1986 National Research Council and Surgeon General's Reports, namely, that data on the issue of ETS exposure and cardiovascular effects are methodologically weak and unconvincing.

- There are several reports and reviews, not considered or not adequately taken into account by OSHA, which have addressed the issue of potential cardiovascular responses to ETS.

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- OSHA cites the following epidemiological reports.

  Ex. 8-85, Dobson, et al. (1991)

  Ex. 8-120, Garland, et al. (1985)

  Ex. 8-138, He, et al. (1989)

  Ex. 8-139, Helsing, et al. (1988)

  Ex. 8-142, Hirayama (1984)

  Ex. 8-148, Hole, et al. (1989)

  Ex. 8-154, Humble, et al. (1990)

  Ex. 8-191, Lee, et al. (1986)

  Ex. 8-277, Sandler, et al. (1989)

  Ex. 8-295, Svendsen, et al. (1987)

- **OSHA's discussion of epidemiologic and experimental data does not adequately support claims of an increased risk of chronic heart effects associated with ETS exposure in the workplace. OSHA fails to critically review cited studies; OSHA misrepresents the nature of available data.**

- OSHA addresses the issue of chronic heart effects in the Proposed Rule at Section II.C.4.(e). [59 FR 15978-9]) Epidemiologic literature on this issue is also reviewed in the context of its risk assessment, at Section IV.B. [59 FR 15992]

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- In Section II.C.4.(e), OSHA provides a single paragraph discussion of the epidemiologic studies relating to ETS and heart disease, coming to the conclusion that these studies indicate a "modest impact" of ETS exposure on heart disease, with relative risks in the range of 1.3 to 2.7.

- **Contrary to OSHA's claim, the 11 citations given by OSHA in support of its conclusion do not report a consistent association of ETS exposure (as inferred from spousal smoking) and heart disease risk.**

- In studies where questionnaire estimates were obtained concerning workplace exposure, the data are especially weak on the issue of a possible association of ETS exposure and heart disease risk.

- **OSHA's misleading use of the 11 epidemiologic reports it cites on ETS and heart disease is evident in the manner in which these reports are grouped in Table IV-2.** [59 FR 15993]

- In two instances, once in the "Positive" column and once in the "Equivocal positive trend" column, OSHA cites the same study twice. In the "Positive" column, both Helsing, et al. [Ex. 8-139] and Sandler, et al. [Ex. 8-277] provide essentially the same data on ETS and heart disease. In the

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"Equivocal positive trend" column, Gillis, et al. [Ex. 8-122] report preliminary data later reported by Hole, et al. [Ex. 8-148] Listing all four reports, when only two studies are represented, gives the impression that more "positive" data are available than in fact might be the case.

- It is of special interest that two of the studies on ETS and heart disease cited by OSHA as "positive" or with an "equivocal positive trend" reported data using questionnaire estimates of workplace exposure. However, neither of these studies provides data suggesting an association of workplace ETS exposure and increased heart disease risk.

- One of the studies with workplace data, Dobson, et al. [Ex. 8-85], is categorized by OSHA in Table IV-2 [59 FR 15993] as "Positive." However, in this study, for ETS exposure at work, the odds ratios and 95% confidence intervals were 0.95 (0.51-1.78) for men and 0.66 (0.17-2.62) for women. Dobson, et al. concluded: "The odds ratios for passive smoking at work did not suggest increased risk." (p. 793)

- In another report, categorized by OSHA as having an "equivocal positive trend," Svendsen, et al. [Ex. 8-295] collected a "limited amount" of data on workplace ETS exposure. Study participants were asked about the smoking habits of their

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coworkers. Comparing nonsmokers whose coworkers smoked to nonsmokers whose coworkers did not smoke, the following relative risks (with 95% confidence intervals) were reported for heart disease:

(1) Coronary heart disease death - RR = 2.6 (CI 0.5-12.7)

(2) Fatal or nonfatal coronary heart disease - RR = 1.4 (CI 0.8-2.5)

- Svendsen, et al. also reported data on a potential joint effect of coworker smoking plus spousal smoking, for the endpoint fatal or nonfatal coronary heart disease.

- Relative to nonsmoking men, the following risks were reported.

(1) Both wife and coworkers smoked - RR = 1.7 (CI 0.8-3.6)

(2) Wife smoked, but coworkers did not - RR = 1.2 (CI 0.4-3.7)

(3) Wife did not smoke, but coworkers did - RR = 1.0 (CI 0.5-1.9)

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- **In sum, all relative risks pertaining to workplace ETS exposure (either alone or in combination with spousal smoking) were not statistically significant.**

- OSHA incorrectly lists Hirayama [Ex. 8-142] as a "positive" study in Table IV-2. [59 FR 15993] While one of Hirayama's tables [Table 5, p. 183 of Ex. 8-142] appears to contain a statistically significant risk ratio for one subgroup of nonsmoking women married to smokers, Hirayama did not report an overall relative risk. Using Hirayama's data, however, Lee (Lee, P.N., Environmental Tobacco Smoke and Mortality. Karger, New York, 1992) recently calculated this ratio to be a nonstatistically significant 1.15 (95% C.I.: 0.94-1.42). (Lee, 1992, p. 187)

- Very little weight can be given to the He, et al. study [Ex. 8-138], since it is a minor Chinese-language report based on only 34 heart disease cases. As noted previously, the Sandler, et al. [Ex. 8-277] report is not relevant since it repeats the data in Helsing, et al. [Ex. 8-139] Also, as noted, the Dobson, et al. report [Ex. 8-85], actually reported nonstatistically significant relative risks less than 1.0 insofar as workplace data are concerned. This leaves OSHA's conclusions on increased heart disease risk based on a single "positive" epidemiological study, Helsing, et al. [Ex. 8-139]

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- As is typical of ETS epidemiological studies, Helsing, et al. suffers from weaknesses, such as unreliable ETS exposure estimates, and failure to attempt to control for confounding factors. The issue of unreliable exposure estimates is a particular problem for Helsing, et al., because the smoking status data were collected in 1963 and then used to classify subjects during the 12 years following. Many changes probably occurred in smoking behavior during the subsequent 12-year follow-up. This concern was noted by the authors:

> All smoking data were obtained in the 1963 census, so no provision can be made for changes in smoking habits which we know took place as a result of publicity about health effects of smoking. (p. 921)

- Other changes in the compositions of the households may have occurred during the follow-up period. Although the authors assume that any changes might influence the ETS comparison groups randomly, this is mere speculation:

> We also have no data on changes in the household composition which may have occurred prior to or after 1963. Thus, we implicitly assume that any such changes occurred randomly in the population. (p. 921)

- Although an attempt was made to adjust statistically for some potential heart disease risk factors (age, sex, etc.), no data

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were available on many potentially important risk factors for heart disease, such as diet, exercise, blood pressure and cholesterol:

> We have very little data on other risk factors for arteriosclerotic heart disease in the study population. . . . other factors such as diet and exercise might differ in families with and without smokers; we cannot ignore the possibility that such differences could influence our findings. (p. 921)

- **The epidemiological literature cited by OSHA as providing "positive" evidence of an ETS and heart disease association provides an extremely weak scientific basis for such a claim.**

- After excluding incorrectly cited literature (Sandler, et al.; Hirayama), a small-scale foreign report of uncertain reliability (He, et al.) and research which, in fact, challenges a workplace ETS exposure/heart disease claim (Dobson, et al.), OSHA is left with a single supporting citation (Helsing, et al.), which itself is highly flawed.

- The problems with Helsing, et al. are particularly troublesome for OSHA's case, because OSHA's risk estimate for heart disease deaths associated with ETS [Section IV.D., 59 FR 15995-6], depends entirely on the Helsing, et al. data for its relative risks.

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- OSHA ignores or glosses over the Helsing study's weaknesses relating to ETS exposure, classification of smoking status and confounding factors. Furthermore, without adequate foundation, OSHA states matter-of-factly that the Helsing, et al. study "can be generalized to the general public," conveniently failing to acknowledge that the Helsing, et al. study was performed in a single county in a single state in the U.S.

- In addition to epidemiologic reports, OSHA also uncritically cites a number of laboratory and clinical reports or reviews, many of which were designed to examine active smoking and do not even relate to ETS. Other studies which purport to relate to ETS are cited by OSHA as fact without any serious attempt to evaluate their scientific validity.

- OSHA provides a substantial amount of detail concerning a recent study said to show that ETS exposure increases myocardial infarct size in rats and increases atherosclerosis in rabbits. In this context, OSHA incorrectly describes a 1993 report by Zhu, et al. [Ex. 8-330] as relating to infarct size in rats, when, in fact, Ex. 8-330 is a rabbit study of atherosclerosis.

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- The rat infarct study described by OSHA appears to be a 1994 report by Zhu, et al.[3]

- Neither the 1994 Zhu, et al. report on rat infarcts, nor the report on atherosclerosis in rabbits cited by OSHA [Ex. 8-330] meet basic standards of scientific control. Both involve excessively high levels of smoke exposure, which was sidestream smoke, not ETS. The conditions of exposure also left a stress factor uncontrolled, which is particularly important in heart disease research.

- To examine the 1994, Zhu, et al. report in more detail, it is clear that it is not even relevant to ETS. It apparently involved simultaneous exposure of groups of rats, up to 24 at a time, to extremely high levels of sidestream smoke, not ETS, in an unventilated exposure chamber. The average air levels of nicotine (1103 μg/m) and carbon monoxide (92 ppm) are several orders of magnitude higher than would be observed in even the most extreme human smoking situation. Moreover, a group of confined rats together in a chamber pumped full of smoke to the point where breathing was almost impossible is going to experience stress in direct proportion to the extent

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3. (Zhu, B., Sun, Y., Sievers, R.E., Glantz, S.A., Parmley, W.W. and Wolfe, C.L., "Exposure to Environmental Tobacco Smoke Increases Myocardial Infarct Size in Rats," Circulation 89(3): 1282-1289, 1994.)

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of exposure. Any test for myocardial infarction is going to be influenced by such a stress factor. In short, the Zhu, et al. study is probably more of a study of stress than a study of ETS.

- In an effort to support OSHA's claim that ETS adversely affects "blood components," OSHA denotes nearly half a column to a 1985 report by Olson. [Ex. 8-245] Olson reports that excessive exposure to intense levels of only weakly diluted sidestream smoke in rats can substantially elevate COHb levels. However, the Olson report did not even pertain to heart disease; it was a study of lung enzymes. It involved high concentrations of sidestream smoke, not ETS, which is a highly dilute mixture. Furthermore, it is clear that the exposure conditions were not relevant to COHb levels associated with ETS, when even literature cited by OSHA indicates that COHb levels in ETS-exposed nonsmokers are essentially indistinguishable from nonexposed nonsmokers. [Guerin, et al., Ex. 8-129, discussed under "Acute Effects."]

- The Davis, et al. report [Ex. 8-80] on platelets and endothelial cells is again cited, despite its lack of an adequate control condition.

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- OSHA cites two Czechoslovakian reports to support a claim that ETS exposure affects cardiac cellular metabolism. [Gvozdjakova, et al., 1984, Ex. 8-130; Gvozdjakova, et al., 1985, Ex. 8-131] Both of these studies are from the same laboratory and involve an experimental model in which rabbits were apparently exposed to mainstream cigarette smoke for periods of up to eight weeks. The authors claim that this smoke exposure adversely effected myocardial mitochonchial respiration. This is suggested as a mechanism underlying cardiomyopathy in smokers. Although the model involved "passive" inhalation of smoke by the rabbits, it is clear from the levels and nature of smoke delivery, and from the authors' explicit comments, that this research was intended to apply directly to heart disease in smokers, not to ETS.

- Benowitz (1991) [Ex. 8-25] is cited several times to support claims about nicotine and carbon monoxide. This citation, however, does not deal with ETS. It is a review of nicotine in the context of smoking and delivery of nicotine via nicotine gum or via transdermal patches. Likewise, the Muscat, et al. (1991) report [Ex. 8-234] on lipid profiles deals with smokers, not ETS.

- Leone, et al. (1991) [Ex. 4-196] is cited as support for a claim that CO decreases ventricular fibrillation threshold.

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The Leone, et al. report did not provide data on ventricular fibrillation, much less any data about CO and ventricular fibrillation in particular.

- **In conclusion, OSHA's discussion of cardiovascular effects is replete with incorrectly cited literature, misinterpreted or uncritically-examined studies and blatant errors as to the relevance of OSHA's citations to the claims advanced.**

- **OSHA has clearly and unquestionably failed to make its case that ETS exposure in the workplace is associated with heart disease risk.**

* * * * * *

- **OSHA omits a number of relevant reviews and studies from the Proposed Rule; these references further undermine claims that ETS exposure in the workplace is associated with a significant risk of heart disease.**

- The literature contains several literature reviews which conclude that a potential relationship of ETS exposure and heart disease has not been established. In view of the highly limited data on workplace ETS exposure, it is not surprising

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that none of these reviews provide conclusions specifically focusing on the workplace.

- However, these reviews do address broad problems with the ETS/heart disease data. If such data are generally inconclusive, then they are reasonably viewed as also specifically inconclusive in regard to the workplace. OSHA failed to recognize the conclusions of these reviews.

- **U.S. Department of Health and Human Services (1986):** This review examined the available data and judged that "no firm conclusion" (p. 10) could be made regarding a possible relationship between ETS and heart disease.

- **Committee on Passive Smoking, Board on Environmental Studies and Toxicology (1986):** This committee report stated that any potential heart disease risk related to ETS would be "difficult to detect or estimate reliably" from epidemiological studies, and would be "the same order of magnitude as what might arise from expected residual confounding due to unmeasured covariates." (p. 263)

- **Wexler, L.M. (1990):** At a ETS conference held at McGill University in 1989, Lawrence Wexler, of the New York Medical College, concluded that recent data did not provide a basis

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for altering the earlier conclusions by the Surgeon General and National Research Council concerning ETS and cardiovascular disease:

> Based on the available evidence, it is this author's opinion that it has not been demonstrated that exposure to ETS increases the risk of cardiovascular disease. (p. 139)

- **Weetman, D.F. and Munby, J. (1990):** Two scientists from the University of Sunderland, United Kingdom, reviewed the literature on ETS and heart disease and presented their conclusions at an international conference on indoor air quality held in Lisbon, Portugal in April 1990:

> It is concluded that no increased risk of cardiovascular disease can be associated unequivocally with exposure to ETS, and it seems probable that this will continue to be the case until specifically designed trials are instigated, and some objective measure of degree of exposure can be devised. (p. 215)

- **Weetman, D.F. (1993):** In a subsequent conference, which addressed a variety of reported risk factors for heart disease in nonsmokers, Professor Weetman again reviewed the ETS and heart disease issue. His review focused on the epidemiological literature, and emphasized that major flaws in the available studies made it impossible to draw conclusions

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as to any possible association of ETS exposure and heart disease:

> It is not possible to conclude that a risk to cardiovascular health has been established from the epidemiological studies considered in this paper. Each of the studies is flawed in at least one major way. If there are to be more studies, and the importance of cardiovascular diseases suggests there should be, one can only hope that they will be conducted in a careful and objective way. (pp. 134-135)

- **Thiery, J. and Cremer, P. (1990):** Two physicians from the University of Munich, Germany, presented their conclusions at an international conference in Hungary in June 1990:

> Taking into account the small increase in coronary risk in passive smokers as compared to non-exposed subjects and also the low validity and small number of epidemiological studies available and the fact that their results are at least inconsistent, a relationship between passive smoking and cardiovascular diseases cannot be established on these data. (p. 6)

- **Armitage, A.K. (1991):** In a 1991 book discussing a wide range of issues involving ETS, the literature on heart disease was reviewed by Alan Armitage, former director of toxicology of a major European research laboratory and head of pharmacology at the Tobacco Research Council Laboratories in the United

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Kingdom. He judged that the scientific data have not established an increased heart disease risk in nonsmokers exposed to ETS:

> It is clear that the evidence for a harmful effect of ETS in enhancing CHD [coronary heart disease] risk in non-smokers is not very convincing. . . . (p. 114)

- **Armitage, A.K. (1993):** In a subsequent review in 1993, Armitage, writing as a consultant pharmacologist and toxicologist, expressed a similar evaluation of the ETS/heart disease literature:

> On the current evidence a causal relationship between exposure to ETS and the development of CHD has not been proved. (p. 27)

- **Caldwell, A.D.S. (1993):** Armitage's 1993 review appeared in the Journal of Smoking-Related Diseases. In an editorial in the same journal issue, A.D.S. Caldwell, the journal's managing editor, emphasized that the issue of confounding variables was of particular importance in the case of heart disease. This is because of the hundreds of factors reportedly associated with the disease. Caldwell observed that the numerous heart disease risk factors make it extremely

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difficult to make confident statements about a potential role of ETS:

> But assessing the impact of ETS is an exercise made hazardous by confounding variables lurking around every statistical corner. In the case of CHD, for example, some 300 risk factors have at some time or other been identified -- by what means is it possible to unravel these data and point the finger with any degree of confidence at ETS per se as a major causative element?

- **Lee, P.N. (1991):** In 1991, Peter Lee, an independent British statistical consultant, published a critical analysis of the epidemiological literature relating to ETS exposure, cancer and heart disease. In the area of heart disease, he was particularly critical of the risk assessments by Wells (1988) and Kawachi, et al. (1989). Both of these risk assessments concluded that ETS is associated with a large number of heart disease deaths annually.

- Lee challenged this conclusion, and agreed with the 1986 National Academy of Sciences and Surgeon General's reports, in that both considered the ETS/heart disease data inadequate:

> In the risk assessment by Wells, heart disease deaths formed 70% of the total. In that by Kawachi et al, they formed 89%. As noted above, in 1986 none of the major authorities considered that ETS had been shown to cause

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heart disease. Evidently Wells and Kawachi, in assuming that ETS causes heart disease, are jumping to a conclusion that a number of panels of distinguished scientists have not reached. While there are more data now than in 1986, it remains abundantly clear that the evidence still does not support this conclusion. (p. 199)

Although it has been demonstrated above that the risk assessment for heart disease essentially rests on the results from two studies, both of which seem unreliable, a number of other general points can be made. First, there are a very large number of risk factors for heart disease. It is evident that adjustment for these factors in the studies has always been incomplete, and often seriously incomplete. Second, the extent of the association seen in some of these studies, which in some cases is close to that reported in relation to active smoking, is implausibly high when viewed against the extent of the association seen in relation to active smoking. Third, there is a major danger of publication bias. It is notable that the literature is still relatively sparse despite the numerous ongoing studies of heart disease and the fact that heart disease in a non-smoker is probably 50 times or so more common than lung cancer in a non-smoker. (p. 200)

- **Lee, P.N. (1992):** In 1992, Peter Lee published a more detailed, book-length review of the epidemiological literature on ETS exposure in relation to mortality and several diseases. In his view, various weaknesses and biases in the data precluded the ability to draw any conclusion as to the potential association of ETS exposure and heart disease:

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> Mainly because of the problems caused by the strong likelihood of severe publication bias, it cannot be concluded from the existing evidence that ETS is associated with heart disease. The present author understands that the American Cancer Society intends to publish within the next year or so findings related to ETS based on its second large prospective study. It is hoped that results from its first prospective study will also be released. Until there is such evidence, and hopefully also evidence from other studies involving substantial numbers of deaths from heart disease with good control of confounding and with evidence on ETS exposure from sources other than the spouse or in the home, it is certainly premature to come to any conclusions. (pp. 195-196)

- **Huber, G.L. Brockie, R.E. and Mahajan, V.K. (1992):** Gary Huber, M.D., of the University of Texas Health Center, in collaboration with two other physicians, recently reviewed the literature relating to claims that ETS is associated with increased heart disease risk. These authors described the epidemiological studies as "inconsistent" and considered the magnitude of the risks reported in these studies to be "within the range of 'background noise.'" Huber, et al. also emphasized the point that potential confounding variables have not been adequately controlled in studies of ETS exposure and heart disease:

> The studies should be viewed with healthy scientific skepticism because they have not been controlled adequately for numerous

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confounding factors potentially important to the development of these diseases. (p. 32)

- **Aviado, D.M. (1992):** In 1992, Domingo Aviado, M.D., a consultant with Atmospheric Health Sciences in Short Hills, N.J., published an extensive review of environmental tobacco smoke in the context of heart disease in the workplace. He did not consider the data supportive of an association of workplace ETS exposure with heart disease, and emphasized the low levels of ETS constituents to which workers might be exposed:

> It is the opinion of this author that the available studies do not support a judgment that ETS exposure is associated with any form of occupation-related heart disease. Although ETS reportedly contains constituents that have been associated with occupational heart disease, the concentrations are so low that it is unlikely for any substance to attain the corresponding TLV (threshold limit value) in a work environment. (pp. 475-476)

- **Aviado, D.M. (1993):** In 1993, Dr. Aviado again addressed this issue, concluding that "the available studies do not support a judgment that ETS exposure is associated with any form of occupation-related heart disease." (p. 130)

- **Crépat, G. (1992):** G. Crépat, a scientist at the University of Dijon, France, reviewed the literature relating to ETS

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exposure and heart disease in a presentation at an international indoor air quality meeting in Athens, in April 1992. He concluded that the relative risks for ETS and heart disease reported in epidemiologic studies have probably been overestimated and are not explained by the available "physiobiochemical" data:

> This suggests that mean RR [relative risk] of CHD due to ETS exposure calculated from available epidemiologic studies, has probably been overestimated as at the moment it cannot be explained by physiobiochemical changes caused by ETS in the body. (p. 440)

* * * * * *

- One way to approach the question of ETS and heart disease is to examine the levels of ETS to which nonsmokers might be exposed. Reported levels of exposure to carbon monoxide may be particularly of interest in view of the potential role some authors have speculated it to have in heart disease.

- The literature emphasizing low levels of ETS constituents provides many examples of reviews concluding that potential nonsmoker ETS or CO exposure levels are extremely low and not likely to be of physiological significance. The conclusions

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of several notable examinations of this issue are extracted below.

- **Adlkofer, F.X., Scherer, G., Von Meyerinck, L., Von Maltzan Ch. and Jarczyk, L. (1989):**

> COHb in passive smokers rises only slightly above the normal physiological level so that it is difficult to differentiate from COHb-values measured in non-exposed non-smokers. (p. 185)

- **Cole, P. (1981):**

> Another source of CO is the inhalation of exhaled tobacco smoke and sidestream smoke from other smokers, called 'passive smoking'. In a City office adjacent to Barts, where smoking was allowed, we measured the COHb levels in 100 non-smokers working alongside active smokers. Again, the mean level was slightly up, 1.12%, but again the increase is hardly significant. Passive smoking, although undeniably unpleasant to some can hardly be described as a health hazard. The rise in COHb does not even approach that found in an active smoker. In the same City office we measured COHb in a 100 active smokers at the same time. They showed a mean level of 5.5% with a maximum of 13%, a completely different picture. We have rarely found a known non-smoker to exceed a level of 2.5% COHb and most are much lower. (p. 76)

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- Gori, G.B. and Mantel, N. (1991):

> The daily levels of cigarette consumption compatible with no significantly increased risk for other diseases associated with active smoking appear to be of the same order as for lung cancer. Tables 4 and 5 report the analogous estimates for cardiovascular and respiratory disease mortality, with the implication that retained doses of ETS are unlikely to be associated with significant risk elevations for such disease as well. (p. 96)

- Table 4 in the paper summarizes data from epidemiologic studies of smoking and heart disease, and provides the "maximum levels of daily cigarette consumption at which risk for coronary heart disease mortality in male smokers may not be significantly increased from the risk of nonsmokers." The maximum levels are in the range of 1.5-4.5 cigarettes per day.

- **By contrast, Gori and Mantel calculate that the average ETS-exposure for a nonsmoker is "less than one cigarette over the course of 1 year."**

> Together, these considerations suggest that the lung cell doses for average ETS-exposed nonsmokers are probably between 1/10,000 and 1/100,000 of equivalent cell doses for average mainstream active smokers. In practical terms, this implies an annual retained dose of tobacco smoke components equivalent to far less than the dose from the active smoking of

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one cigarette somehow evenly dispersed over a 1-year period. (p. 94)

- **Malmfors, T., Thorburn, D. and Westlin, A. (1989):** This is a study of the air quality in passenger aircraft, focusing on components related to ETS. Although no potential health effects were measured, the report emphasizes the low levels of ETS-related components and observes these are unlikely to have an important cardiovascular significance. It is also noted that the nicotine and carbon monoxide levels in aircraft cabins are well below the standards set by OSHA:

> It can be seen that the nicotine concentrations found in the present study are roughly one-tenth of the standard for the working environment set by OSHA. The concentration of carbon monoxide is also about one-tenth of the standard for general indoor air and even less for the working environment. (p. 623)
>
> From this comparison it appears that the quality of the aircraft cabin air in the present study is satisfactory and better for factors related to ETS - nicotine and carbon monoxide - than for carbon dioxide and relative humidity. (p. 624)
>
> Any effects on the cardiovascular system would have been mostly unnoticed in healthy individuals, because there are no known direct effects of ETS on the cardiovascular system beyond the formation of carboxyhemoglobin. The latter is so minimal that it will not affect the cardiovascular function. (p. 626)

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- Proctor, C.J., Warren, N.D., Bevan, M.A.J. and Baker-Rogers, J. (1991):

> It seems that the main factor in exposure to environmental tobacco smoke is living with a smoker. Exposure at work, leisure, or travel seems to be minor. Overall, exposure to airborne nicotine was found to be low (mean 2.3 $\mu g\ m^{-3}$, median $<0.1\ mg\ m^{-3}$). (p. 296)

- Mennear, J.H. (1993):

> The role, if any, of environmental tobacco smoke (ETS) in the causation and/or exacerbation of cardiovascular disease remains to be proven and defined. . . . The findings show that there is scant clinical or experimental evidence to support a role for carbon monoxide in the causation of ischemic heart disease. Further, the results of field studies of relative air quality in nonsmoking and smoking homes, offices, and public places show that ETS contributes only minor and toxicologically insignificant increments in ambient carbon monoxide concentrations. These increments are variable and easily masked by other common carbon monoxide sources such as internal combustion engines and the burning of cooking and heating fuels. It is concluded that if ETS plays a role in the etiology of cardiovascular disease, it is most likely not mediated through carbon monoxide. (p. 77)

- Roe, F.J.C., (1993):

> Although it has not been proven that intermittent low peak levels of COHb do no permanent harm, it seems likely that the

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healthy body can compensate for them completely. (p. 120)

There is no clear evidence that exposure to CO is associated with an increased incidence of any form of cardiovascular disease. (p. 125)

- **Rylander, R. (1983):**

The unimportance of carbon monoxide has been further confirmed. . . . CO from ETS is not important from a health point of view. (p. 144)

- **Schievelbein, H. and Richter, F. (1984):**

Cardiovascular effects of tobacco smoke have been studied in passive smokers far less extensively than in active smokers. Under real-life conditions, passive smokers inhale approximately 0.02 to 0.01 of the amount of particulate matter taken up by active smokers. Their nicotine concentration in serum is within a range that is barely distinguishable from the background level. The increase in carboxyhemoglobin rarely exceed 1%. In healthy subjects heavily exposed to tobacco smoke, no or only slightly acute effects on the cardiovascular system are found. Whether or not passive smoking is likely to aggravate symptoms in patients with advanced coronary heart disease has not yet been unequivocally established and requires further investigation. From a few studies on occupational groups exposed to carbon monoxide (CO) and from experiments with animals chronically treated with CO or nicotine, the conclusion can be drawn that neither CO nor nicotine is likely to play a role in the development and progression of coronary heart

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disease in those concentrations normally found in passive smokers. (p. 626)

- Several aspects of cardiovascular function, such as heart rate and blood pressure, can be readily measured in laboratory studies. Even if short-term changes in such parameters were consistently reported following acute exposure to ETS or CO, their potential clinical significance is highly uncertain.

- On the other hand, if the literature does not consistently report important acute cardiovascular responses, this further undermines claims of a potential relationship between ETS and heart disease.

- A number of studies and reviews have examined potential acute cardiovascular responses to either ETS or CO. A sample of this literature is cited below, indicating a sizeable body of scientific data and opinion questioning a role of ETS or CO in such effects and emphasizing that any measurable acute cardiovascular responses to ETS are minor.

- **Committee on Passive Smoking, Board on Environmental Studies and Toxicology (1986):** The report reviews studies of possible acute effects of ETS on the cardiovascular system in healthy subjects, and concludes that there are no significant changes.

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The report, although avoiding a firm conclusion, expresses that, for angina patients, there is a possible cause for concern about exposure to the CO in ETS:

> In summary, for normal young adult males and females, no significant acute effects of ETS exposure on heart rate or blood pressure have been reported, either under resting or aerobic conditions. (p. 260)

- **Fischer, T., Weber, A. and Grandjean, E. (1978):** Potential subjective, irritant and physiological (e.g., heart rate) effects of ETS were assessed in a laboratory setting. No pulmonary function or heart rate effects were reported. However, the authors nevertheless consider ETS a serious problem in view of irritant effects, potential effects in sensitive persons and levels to which some restaurant and bar employees are exposed:

> Pulmonary function tests should give us an indication of eventual bronchial constriction, encountered frequently in smokers. In fact, our spirometric methods showed no differences before and after exposure to smoke. The change in heart rate during the test was just as insignificant. (uncertified translation, p. 8)

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- **Harke, H.-P. and Bleichert, A. (1972):**

> Measurements of electrocardiogram, blood pressure, and puls [sic] frequency showed, that these parameters were not altered by passive smoking. (p. 312)

- **Hulka, B.S. (1988):**

> Studies of acute ETS exposure in healthy children and adults have shown no statistically significant alterations in heart rate or blood pressure either during resting conditions or during exercise. Studies of ETS exposure in persons with pre-existing atherosclerotic heart disease have been inconclusive. Important questions about ETS exposure and the induction of angina, electrocardiographic abnormalities, and cardiac arrhythmias are unanswered. (p. 537)

- **International Collaborative Group (1984):** This study examined children (approximately 13 years old) from cities in Germany, Cuba, Hungary and the USSR. Two sample groups were compared, one representing the upper 5% and one representing the remainder of the blood pressure distribution curve.

- One of the characteristics compared between these two groups was parental smoking habits. No significant association was reported between the children's blood pressure and parental smoking:

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The proportion of smokers among the fathers was slightly higher in the lower (55.8%) than in the upper group (54.7%); this difference was not significant. The proportion of smokers among mothers was, however, significantly higher in the lower than in the upper group ($P<0.01$). The proportion of smoking fathers was lowest in Berlin-Köpenick (46.3% vs. 38.6%) and highest in Havana (66.3% vs. 66.7%). The proportion of smoking mothers was lowest in Moscow 3 (0% vs. 1.4%) and highest in Budapest (29.4% vs. 32.0%). The mean blood pressure values of the children showed no significant association with the smoking habits of either parent. (p. 122)

- **Pimm, P.E., R.J. Shephard and F. Silverman (1978):**

  It is concluded that in normal subjects the magnitude of physiological responses to acute exposures is minimal. . . . (p. 201)

- **Rummel, R.M., Crawford, M. and Bruce, P. (1975):** Heart rate and blood pressure measurements were made on 17 male and 39 female nonsmoking college students at 5, 10, 15, and 20 minutes during exposure to exhaled cigarette smoke in an enclosed room. . . . Measurements were correlated with attitudes toward smoke exposure.

  For the entire group of nonsmokers, there were no significant changes in heart rate or diastolic blood pressure during the smoke exposure, but systolic blood pressure was significantly

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increased at 5 minutes of exposure; at 20 minutes of exposure it had returned to preexposure values.

When results were examined according to nonsmokers attitudes, those who "disliked" being exposed had significantly greater heart rates than those who were "indifferent" at all measurements; blood pressures between the two groups did not differ significantly.

- **Samet, J.M. (1988):**

> While these effects [relating to oxygen transport, heart and blood pressure increases, etc.] of carbon monoxide and nicotine may impair performance, exposures to environmental tobacco smoke are generally at concentrations below which physiological effects would be expected. (p. 12, col. 1)

- **Shephard, R.J., Collins, R. and Silverman, F. (1979):** The responses of healthy men and women were measured during exercise performance while exposed to ETS vs. a sham exposure. Among several other variables, heart rate was measured. During a preexposure period, those subjects who were to undergo ETS exposure had higher heart rates than the sham subjects. However, actual exposure was associated with a smaller heart rate increase compared to the sham condition:

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> The heart rate was higher before the experimental than before the sham exposures. . . . However, while actually exposed to the cigarette smoke both the increment of heart rate and the absolute heart rate were less than in the corresponding sham exposure. (p. 285)

The authors suggested that these heart rate changes might be related to a subjective anxiety or hyperventilation reaction, rather than an actual physiological response to ETS.

- **Turner, J.A.McM. and McNicol, M.W. (1993):**

> In a partially blind randomized control study, nine healthy adult men performed progressive sub-maximal exercise tests, either after chewing nicotine chewing gun (4 mg) or breathing carbon monoxide (320 p.p.m.). Neither agent significantly affected exercise performance, despite a mean rise in blood nicotine to 17.0 ng ml during nicotine administration and a COHb rise to 6.9% whilst breathing carbon monoxide. (p. 427)

- **Weber-Tschopp, A., Fischer, T. and Grandjean, E. (1976):**

> Thirty three subjects were exposed in a climatic chamber to cigarette smoke (side stream) produced by a smoking machine. . . . $\%FEV_1/VC$, MMF and heart rate were not significantly affected during exposure. (p. 277)

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- **Weber, A., Fischer, T. and Grandjean, E. (1979):**

  In a first study subjects were exposed for 1 hr to constant cigarette smoke concentrations corresponding to 5 or 10 ppm CO. Annoyance, subjective eye irritations, and eye blink rate increase in both conditions during the first 30 min of exposure. Respiratory frequency and heart rate variability are not altered. (p. 205)

- **Winneke, G., Plischke, K., Roscovanu, A. and Schlipkoeter, H.-W. (1984):**

  Neither blood pressure-values, nor heart-rates or fingerpulse-volume were influenced by exposure to tobacco-smoke. This correspond to the fact that nicotine-intake from passive smoking is negligible. Depth and rate of breathing were not altered either. (p. 353)

  As for carbon monoxide (CO) there was pronounced uptake in terms of COHb for the high exposure-condition only. In absolute terms, however, the measured values correspond to those found in non-smoking urban populations, and are well below levels considered critical for persons with cardio-vascular impairment. (p. 354)

- **Winneke, G., Neuf, M., Roscovanu, A. and Schlipköter, H.-W. (1990):** Physiological measurements were obtained from nonsmokers, while they were in an exposure chamber in which another individual was smoking. No significant effects were reported for heart rate or blood pressure. The authors

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reported that "cardiorespiratory variables were not affected by ETS exposure." (p. 173)

> In taking CO as the basis for comparison our cardiovascular findings are consistent with those of others, who, at even higher levels of ETS-exposure did not observe exposure-related increase of either heart-rate or blood-pressure. Nicotine-intake at such ETS-levels is likely to be too low for cardiovascular changes to be expected. (p. 181)

- Regarding angina and other heart disease patients, claims are sometimes made that ETS, or specifically CO in ETS, aggravates cardiovascular disease in people with pre-existing illness. Such claims typically stem from a limited and largely discredited report by Wilbert Aronow that angina patients experienced chest pain sooner when exercising in the presence of ETS.

- **However, a closer examination of the literature reveals a body of data that raises questions about claims that ETS, or CO at levels reported to be in ETS, has significant adverse cardiovascular effects.**

- Hinderliter, A.L., Adams, K.F., Price, C.J., Herbst, M.C., Koch, G. and Sheps, D.S. (1989):

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In conclusion, low-level CO exposure is not arrhythmogenic in patients with coronary heart disease and no ventricular ectopy at baseline. (p. 89)

- **McNicol, M.W. and Turner, McM. (1983):**

> There was no change in the mean oxygen uptake at the onset of angina with any intervention. . . . These results are in contrast with previous reports of the effects of smoking and carbon monoxide on exercise performance in angina pectoris. However in all of these other studies a subjective rather than objective end point was used. We suggest that an objective assessment is essential and that oxygen uptake at the onset of angina is useful and relatively easy to measure.

- **Shephard, R.J., Collins, R. and Silverman, F. (1979):** This study was an attempt to determine if asthmatic subjects have an increased sensitivity to ETS exposure. Respiratory symptoms, pulmonary function and heart rates were measured. Although some slight effects (e.g., a small heart rate increase) were reported, these were considered to be of "doubtful biological importance" and most likely due to an emotional, rather than directly physiological, response to the ETS exposure:

> There was also some evidence of arousal and/or emotional excitement, including a slight tachycardia (at 80-min exposure, $P<0.05$) and a slight increase of forced vital capacity

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(P<0.05 at 90-min exposure). However, dynamic lung volumes . . . were unaltered. . . . Our data thus do not suggest that asthmatic subjects have an unusual sensitivity to cigarette smoke. (p. 392)

The physiological changes observed in normal subjects during smoke exposure, although occasionally reaching conventional levels of statistical significance, were of doubtful biological importance (Pimm et al., 1978; Shephard et al., 1979a). Findings included some increase of heart rate and respiratory minute volume, probably of emotional origin, a tendency of increase in functional residual capacity and residual volume in some experiments, and small decreases of dynamic lung volumes. The asthmatic subjects also showed emotional reactions to the cigarette smoke, including the tachycardia, and possibly the preexposure increase of FRC and TLC. (pp. 399, 401)

We would thus conclude that the specific sensitivity of asthmatic subjects is not a major consideration when determining air quality criteria for rooms contaminated by cigarette smoke. (p. 402)

- **Sheps, D.S., Adams, K.F., Bromberg, P.A., Goldstein, G.M., O'Neil, J.J., Horstman, D. and Koch, G. (1987):**

In conclusion, there is no clinically significant effect of 3.8% COHb (representing a 2.2% increase from resting values) on the cardiovascular system in this study. (p. 108)

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IRRITATION

- The proposed rule does not correlate complaints of irritation with actual workplace exposures to ETS, and fails to demonstrate that current ETS exposure levels in the workplace pose a significant risk of material health impairment from "irritation."

- OSHA's Proposed Rule states that "mucus membrane irritation" is part of "a wide spectrum of health effects . . . associated with exposure to ETS." [59 FR 15973] In support of its claim that ETS is an "irritant," OSHA cites a single summary review of the literature (1986), two studies and six personal testimonials submitted to the OSHA RFI docket. [59 FR 15975]

- The Proposed Rule also lists several substances that have been defined as "irritants" by NIOSH and are reportedly found in tobacco smoke, but OSHA concedes that specific constituents in ETS have not been directly related to irritation effects. [59 FR 15987-8, 15975]

- The two studies on ETS and irritation cited in the Proposed Rule do not establish a significant risk of material health impairment at current workplace exposure levels. The data in one of the studies cited in the Proposed Rule were collected

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in Switzerland in the late 1970s, and the high levels of respirable particulate matter reported therein are not relevant to current ETS exposure levels in the U.S. [Ex. 4-317] Moreover, the Proposed Rule does not address the authors' qualifications of the data in the study, i.e.,

> . . . there is a very poor correlation between the mean pollutant concentrations in each room and the corresponding results of the interview. This means that the measured pollutant concentration in an individual work room does not necessarily allow drawing conclusions on the extent of disturbance and irritations . . . .;
>
> Individual psychological factors (relationship with co-workers, work satisfaction, attitude toward smoking) considerably influence individual evaluation of disturbances and irritations . . . .;
>
> Thus, there is a considerable variance on the side of measurements of chemical and physical properties as well as on the side of subjective perception and feelings.

- A second study cited in the Proposed Rule was conducted in Japan in the mid-1980s. [Ex. 4-18] Subjects were exposed to extremely high levels of tobacco smoke in an experimental chamber. The peak level of exposure to respirable particulate matter was nearly 100 times greater than levels encountered in workplace situations where smoking is permitted.

- The relevance of this experimental study to OSHA's claim about irritation is unclear; Benzene explicitly prohibits OSHA from

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basing its finding of "significant risk" at "lower levels of exposure . . . using evidence of health impairments at significantly higher levels of exposure." (AFL-CIO v. OSHA, 965 F.2d 962, at *978)

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- In the introduction to its standard governing workplace exposure to air pollutants, OSHA summarizes its authority as follows:

> Some impairments are so slight a discomfort that they are not material and do not provide a basis for regulation. A complaint of minor discomfort, in and of itself, is not material impairment. However, the OSHA Act is designed to be protective of workers and is to protect against impairment with less impact than severe impairment. [54 FR 2332, 1989]

- OSHA also states:

> . . . [C]omplaints of minor irritation would not in and of itself constitute material impairment. In addition, OSHA would weigh irritation with physical manifestations more heavily than irritation with purely subjective responses. This does not mean that purely subjective responses would not constitute material impairment. That judgment would depend on the magnitude of the irritation. [54 FR 2362, 1989]

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- If OSHA is to support its claim that irritation from exposure to ETS is a material impairment, it must demonstrate that exposures bring about something more than subjective responses of minor irritation or annoyance, i.e., it must demonstrate the "magnitude" of the purported irritation effect.

- **OSHA must demonstrate the "extent of the risk posed by individual substances," i.e., that existing exposure levels in the workplace pose a significant risk of material health impairment (due to irritation). It also must provide an "assessment of the level at which significant risk of harm is eliminated or substantially reduced."**

- OSHA will find little, if any, support for its position in the scientific literature. For instance, the major databases on sick-building syndrome indicate that tobacco smoke is rarely the underlying cause of complaints about irritation and annoyance related to indoor air quality. [Exs. 3-1053, 3-1073, 3-1074]. ETS has been identified as a source of claimed discomfort in only two to five percent of a combined total of 1,000 sick-building investigations.

- Other published investigations of workplace venues report similar results. For example, in 1992, Canadian researchers reported results of a building investigation in which

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temperature, humidity, dust, nicotine, formaldehyde, volatile organic compounds, and CO_2 were measured. Occupants of the building complained of poor indoor air quality, and a questionnaire evaluation revealed a substantial number of complaints about unsatisfactory thermal conditions, dry air, drowsiness and eye irritation. However, all measured parameters, including temperature and humidity, were within accepted comfort/exposure guidelines. The authors were unable to correlate any single measured environmental parameter with complaints or symptoms.

- They concluded that their investigation "showed that complaints reported by occupants were associated with perceived rather than measured levels of indoor environmental parameters."

- A 1989 report by Hedge, et al. noted that while self-reported exposures to ETS were associated with increases in perceived symptoms of irritation, no significant correlations between actual levels of ETS constituents in the indoor air and symptom prevalence could be established. Moreover, the researchers reported that "passive smoking" was not associated with self-reports of mucus membrane irritation (MMI).

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- Pimm and co-workers examined the effects of ETS exposures "at levels typically encountered in public buildings" in the late 1970s. Physiological parameters such as lung flow rates, heart rates and blood carboxyhemoglobin levels were measured. The researchers reported that "the magnitude of the changes was small and of questionable biological significance."

- The authors also observed that "the subjects were also inevitably aware of the presence of the smoke, and the reported reactions may have been influenced by underlying beliefs and attitudes." Subjective complaints of irritation were categorized as "symptomatic" rather than physiological.

- The Proposed Rule rejects the possibility that complaints about indoor air quality, and specifically complaints about ETS, may be mediated by a psychological component and suggests only that a "psychological overlay" may be common to complaints related to poor indoor air quality. [59 FR 15970]

- **Research indicates that the mere visibility or presence of ETS may provoke symptoms and complaints.**

- Winneke and colleagues found that aversion to ETS increased the degree of annoyance and irritation reported under experimental exposure conditions. Researchers from the

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Illinois Institute of Technology in 1992 reported that simple visual contact "with a source of tobacco odors" increased both perceived odor intensity and the number of subjects perceiving tobacco odor.

- Other recently published studies have demonstrated the importance of variables such as job stress, including work control, support, possibilities for personal growth and job satisfaction, in the perception of symptoms due to sick-building syndrome. The studies suggest that such factors may either be directly related to symptoms as stress reactions, or they may play a role in rendering the individual more prone to react to environmental influences, including perceived exposures to ETS.

- ETS is easily identified and is often blamed as the cause of complaints of annoyance and irritation, especially among individuals who dislike tobacco smoke. However, a workplace that is adequately ventilated with outdoor air effectively addresses and prevents complaints of irritation and annoyance, regardless of the suggested source.

- ASHRAE ventilation Standard 62-1989 was developed in order to minimize potential complaints of annoyance and irritation in indoor environments. The ventilation rates in the Standard

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specifically address ETS. The Standard's design criteria currently apply to buildings that have been constructed, renovated or remodeled in the U.S. after 1990. Indeed, the Standard is incorporated by reference into OSHA's Proposed Rule on IAQ. [59 FR 16036]

- **OSHA's Proposed Rule calls for the complete elimination of ETS exposure in the workplace. This proposal, of course, will not eliminate exposure to irritants in the workplace, since precisely the same irritants imputed to tobacco smoke by OSHA are emitted from other sources. [59 FR 15987-8, 15984]**

- **The levels of "irritants" found in the indoor air of the nonindustrial workplace typically overwhelm any possible contributions from tobacco smoke.**

- For example, Godish, in his review of formaldehyde exposures from tobacco smoke, writes that even under "extreme circumstances, the effect of cigarette smoking on formaldehyde levels in indoor spaces would be negligible. Guerin, et al., similarly conclude that "as such, it has been difficult for many studies to demonstrate consistently elevated levels of formaldehyde due to ETS." [Ex. 8-129, also submitted to OSHA as Ex. 3-499]

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- They also conclude: "Studies of offices, restaurants, train compartments, and public buildings suggest that ETS contributes to the indoor air burden of VOCs but that other sources predominate. Major sources include building materials, furnishings, cleaning products, office machines, gasoline, and combustion sources associated with cooling, heating, and transportation."

- These results indicate that contributions from ETS to ambient levels of "irritants" are minimal and often indistinguishable from background levels. Any potential risk from irritation associated with ETS therefore would be addressed with the implementation of OSHA's own Proposed Rule on indoor air quality (a ventilation-based indoor air quality standard).

- **OSHA's record is devoid of any data suggesting that ETS is an irritant under current workplace exposure levels and/or under conditions of adequate ventilation (e.g., outdoor air rates specified in ASHRAE 62-1989).**

- OSHA's proposal to reduce alleged irritation from ETS through the complete elimination of smoking in the workplace is equivalent to the "regulation of insignificant risks."

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PULMONARY EFFECTS

- **OSHA presents data which are irrelevant to a discussion of potential pulmonary effects in nonsmokers exposed to environmental tobacco smoke in the workplace.**

- OSHA's task is to show that there is a significant risk of material health impairment in nonsmokers exposed to environmental tobacco smoke in the workplace. OSHA, however, bases its "review" of pulmonary effects on one experimental study [Ex. 8-18] in humans as well as on several epidemiological studies [Exs. 8-37, 8-62, 8-148, 8-173, 8-176, 8-178, 8-180, 8-209, 8-210, 8-278, 8-295, and 8-321], most of which examined reported exposures to ETS in the home environment. OSHA also discusses several animal inhalation studies. [Exs. 8-322, 8-204, 8-290, 8-104, 8-45, and 8-114] OSHA concludes the following:

> The weight of the evidence shows that exposure to ETS results in decreases in pulmonary function indices and increases in respiratory symptoms in otherwise healthy men and women who are exposed to ETS for periods of 10 or more years. [Emphasis added; 59 FR 15977]

- **Because there are studies available that have examined potential effects of exposure to ETS on the respiratory health**

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of nonsmoking adults in the workplace, those are the studies which should be reviewed and analyzed in this section. OSHA presents no critical discussion of the data available from these studies and makes no scientifically supportable claims regarding causation.

- Recent reviewers of the pulmonary effects literature (who are affiliated with the International Agency for Research on Cancer) concluded that "on the basis of the available data, no definite conclusion (excluding the acute irritating effect of ETS on respiratory mucous membranes) can be drawn." The reviewers' conclusions were not discussed in the Proposed Rule.

* * * * * *

- **OSHA relies on an experimental exposure chamber study which did not examine or make any conclusions regarding respiratory endpoints in nonsmokers exposed to ETS.**

- OSHA cites a 1983 study by Asano, et al. [Ex. 8-18] This study was an experimental exposure chamber study of only 20 subjects, including 5 male smokers, 5 male nonsmokers and 10 female nonsmokers. It is unclear why OSHA included this study in the pulmonary effects section, since the study reports on

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non-pulmonary endpoints such as systolic blood pressure and heart rate. **This study is therefore irrelevant to a discussion of potential pulmonary effects in nonsmokers exposed to ETS in the workplace.**

* * * * * *

- **OSHA relies on survey reports of nonsmokers who live with one or more smoker(s); these studies suffer from important flaws, and do not constitute the "best available evidence" regarding potential pulmonary effects in nonsmokers exposed to ETS in the workplace.**

- The epidemiological literature upon which OSHA bases its conclusion suffers from a couple of very important problems. First, very few of the studies report on <u>workplace exposures to environmental tobacco smoke</u>, the very issue OSHA is proposing to regulate. Second, the studies contain no actual exposure data. In the majority of studies, the estimation of exposure originates from questionnaire responses of subjects and/or their spouses and co-habitants. Even though the studies suffer from these problems, the magnitude of the reported decrements in pulmonary function in healthy nonsmokers reportedly exposed to environmental tobacco smoke,

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as OSHA itself concedes, is very small and of questionable biological or clinical significance.

- Among the epidemiologic studies OSHA chose to rely on are several studies of reported home exposures to ETS. The 1985 study by Brunekreef, et al. estimated exposure of nonsmoking women in the Netherlands by asking the subjects to quantify the number of cigarettes smoked daily inside the home by household members. While this study, on cross-sectional analysis, reported that several pulmonary function parameters appeared to be significantly associated with exposure to ETS in the home while others did not, the authors also reported that "there was no association between [ETS] exposure and pulmonary function decline." [Ex. 8-37]

- Another study referenced by OSHA, a 1981 paper by Comstock et al., examined reported home exposures of 1,724 adults to environmental tobacco smoke. [Ex. 8-62] The authors of this study, epidemiologists at the Johns Hopkins University School of Medicine, reported:

> The presence of a smoker in the household other than the subject <u>was not associated with the frequency of respiratory symptoms, and only suggestively associated with evidence of impaired ventilatory function</u>. [Emphasis added]

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- A 1989 study by Hole, et al., is also cited by OSHA. [Ex. 8-148] In this paper, "passive smoking" was defined as living at the same address as a smoker. Additional attempts to quantify exposure involved questioning subjects regarding the number of cigarettes smoked daily by their co-habitee.

- While this study reported associations between living with a smoker (as a surrogate of ETS exposure) and several respiratory health endpoints in nonsmokers, the 95% confidence interval fell below unity for all respiratory endpoints (i.e., the associations were not statistically significant).

- In the Letter to the Editor written by Kalandidi in 1987, which informally reports on a study the author was conducting in Greece that suggested exposure to environmental tobacco smoke "may contribute to the cause of COLD [chronic obstructive lung disease]," the author writes that the studies on exposure to ETS and adult respiratory health contain data that are "equivocal." [Ex. 8-173]

- In 1990, Kalandidi reported these data in a published paper. While the data were suggestive of a possible association, it is questionable whether the authors adequately considered other potential exposures which have been associated with the

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development of COPD such as the extremely high levels of outdoor air pollution found in Greece.

- OSHA cites two studies by Kauffman, et al. The first study, published in 1983, reports on home exposures to ETS of nonsmoking women married to smokers. [Ex. 8-176] The second study, published in 1989, reports on similar data. [Ex. 8-178] While the authors reported an association between decreased lung function and "passive smoking" in French women, the authors reported that "no significant association between passive smoking and level of lung function" was apparent in American women.

- Dr. Michael Lebowitz (a member of the EPA's Science Advisory Board Committee which reviewed the EPA's Risk Assessment on ETS) has questioned the conclusions of the Kauffman study [Ex. 8-176], which, as mentioned above, reported significant differences in lung function between exposed and nonexposed nonsmokers in one part of the study population but no significant differences in the population as a whole. Dr. Lebowitz noted that since the "healthiest" part of the study population lived in the most polluted areas, the study may have been flawed due to biased population selection and testing for other confounding factors.

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- Since OSHA decided to rely on epidemiologic studies of reported ETS exposures in the home, studies of reported home exposures not cited by OSHA in its proposed rulemaking warrant mention. In 1983, for example, Jones, et al., reported that in a case-control study of several hundred nonsmoking women from a U.S. study population, there was no significant association between decreases in lung function and exposure to ETS in the home. Similarly, Lebowitz, et al., coordinators of an epidemiologic study of obstructive lung disease in Arizona, reported no association between reported ETS exposures in the home and respiratory health in their adult study population. In a study of 376 families, Yale University scientists Schilling, et al., also reported no evidence that environmental tobacco smoke affects either lung function or respiratory symptoms in adults.

- Similarly, OSHA failed to discuss various government reviews of the ETS and adult respiratory health literature which have generally concluded that there is a negligible association, if any, between exposure to ETS and respiratory health effects in adult nonsmokers.

- For example, the 1986 Surgeon General's report on ETS concluded:

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> Healthy adults exposed to environmental tobacco smoke may have small changes on pulmonary function testing, but are unlikely to experience clinically significant deficits in pulmonary function as a result of exposure to environmental tobacco smoke alone.

- Other researchers who have analyzed these reported data contend that the results are "mixed and inconclusive." For example, researchers in France, Laurent, et al., have commented that purported long-term health effects from exposure to ETS are difficult to demonstrate in healthy adults and that the results of the epidemiological studies are "sometimes conflicting and often open to question." One investigator who is critical of ETS conceded that "the effect of passive smoking on respiratory infections in adults has not been well characterized and reports of its effects on chronic respiratory disease in adults have been inconsistent."

- In his summary of the studies on respiratory symptoms and diseases in adults published up to early 1990, American investigator Dr. Philip Witorsch noted that while "4 of 8 [reported] an increased frequency, 4 of 8 [reported] no increased frequency." He stated that, in addition to "all of the problems" with the studies, "these results are too variable to permit any conclusion of association." As his summary demonstrates, the conclusion of the participants at

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the 1983 U.S. National Institutes of Health workshop on ETS exposure, that the possible effect from ETS "varies from negligible to quite small," is still pertinent.

* * * * * *

- **The epidemiologic studies which examined reported workplace exposures to ETS in nonsmoking adults have reported inconsistent and inconclusive data.**

- **The study upon which OSHA places the most weight has received substantial criticism in the scientific literature for questionable data acquisition and analysis.**

- OSHA reports on four studies which contain discussions of workplace exposures to ETS. Probably the most familiar study mentioned in this section is the 1980 White and Froeb study. [Ex. 8-321]

- While this study is often cited by individuals in support of an association between exposure to environmental tobacco smoke in the workplace and small airways dysfunction in healthy nonsmokers, the study has received substantial criticism in the published literature. OSHA does not address any of these criticisms in its Proposed Rulemaking.

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- In regard to the White and Froeb study, a physician at a U.S. medical school questioned their use of carbon monoxide as an index of smoke exposure, contending that they "do not have reliable estimates of the smoke exposure in the environment of their nonsmokers" because it is not unique to tobacco smoke. A British reviewer shared the physician's view that White & Froeb's findings "relate to an index which is contentious and certainly not an accepted reliable indicator of an increased health risk." White and Froeb themselves noted that the average values of the pulmonary tests of nonsmokers exposed to tobacco smoke "were not notably different" from the values suggested as normal by a specialist in this area.

- Perhaps the most telling criticisms of the White & Froeb study were voiced by Dr. Michael Lebowitz of the University of Arizona at an annual joint meeting of the American Lung Association/American Thoracic Society and in a subsequent letter published in the U.S. Congressional Record. During a forum at the ALA meeting, Dr. Lebowitz stated that he had concluded, from his own extensive review of the study and from an interview with White, that the study was "improperly designed" from an epidemiological point of view. He noted that there were problems "inherent" in the study, including the selection of the study group and the measurement of smoke in the workplace.

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- Dr. Lebowitz also expressed concern that the statistical significance of the data appeared to depend on the unexplained omission of data for 3,000 people who were originally included in the study. Based upon these considerations, Dr. Lebowitz urged that the study not be used to support the claim that exposure to ETS in the workplace affects the lung function of healthy nonsmoking adults.

- Dr. Lebowitz again took issue with the White and Froeb study in a 1984 paper he presented at the Vienna Symposium on Passive Smoking. He contended:

> Even with a biased population, poor study design, and incorrect statistical evaluation, there were no clear-cut, consistent, medically meaningful differences between passive smokers and groups of nonsmokers; a corrected statistical analysis strengthened this conclusion.

- Fielding and Phenow, whose conclusion that the "changes" reported by White and Froeb were "equivalent to those found in light smokers, who smoke from 1 to 10 cigarettes per day" is reported by OSHA, also made several highly relevant statements that are not mentioned by OSHA. [Ex. 8-102]

- Fielding and Phenow suggest that the data from the studies on ETS exposure and adults "have been conflicting" and that

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"taken together, the limited data on the effect of [environmental tobacco] smoke on adult lung function are inconsistent and inconclusive."

- The data from the White and Froeb study appear to be inconsistent with other data on lung disease and lung function in nonsmokers. For example, a 1984 study of 1,351 German office workers by Kentner et al., reportedly found no effect of ETS on pulmonary function among exposed nonsmokers. [Ex. 8-180] In a 1988 update of the study, the investigators noted that "there is no evidence that average everyday passive smoke exposure in the office or home leads to an essential reduction of lung function in healthy adults." The key investigator reiterated these conclusions in 1989 and 1990 publications. The 1984 study is cited by OSHA in its proposed rule, but no discussion of the study or its data is included.

- Two other studies cited by OSHA which report data on workplace exposures of nonsmoking adults to ETS suffer from serious problems regarding exposure assessment. The Masi (1988) study reported on 293 subjects, aged 15 to 35 years old. [Ex. 8-209] The study, however, contains such crude "exposure" data that it is disturbing that OSHA deems it reliable. Workplace "exposure" to ETS was assessed in the following manner:

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> Bank employees were asked to [subjectively] assess smoke conditions in the work area as light, moderate, heavy or unable to quantify. . . .[these categories] were arbitrarily converted to number of cigarettes. [Emphasis added]

- Similarly, the authors of the Masjedi (1990) study conceded that most of their subjects "were unable to quantify the amount of [their] exposure to passive smoke. . ." [Ex. 8-210]

* * * * * *

- **The epidemiologic and experimental data available do not support OSHA's contention that compromised individuals in the workplace have a significant risk of material health impairment because of exposure to environmental tobacco smoke.**

- OSHA claims that although the pulmonary function decrements reported to be associated with exposure to ETS in healthy nonsmokers are small and of questionable clinical significance, these changes may become significant in persons with already impaired pulmonary function (e.g., asthmatics). In its attempt to substantiate this claim, OSHA references two experimental studies on adult asthmatics exposed to ETS for one hour in an exposure chamber.

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- The first study, Knight and Breslin, 1985, reported on only six subjects, four of whom had previously given a positive history of ETS "attacks." [Ex. 8-182] The authors (and OSHA) did not discuss the possibility that psychological factors may have played a role in the subjects' reported "reactions" to the ETS exposure.

- The second study, by Dahms et al., 1981, reported on ten patients with asthma (five of whom were included because they reported specific complaints when exposed to cigarette smoke) and ten normal patients. [Ex. 8-76]

- While the authors of the second study reported an association between exposure to ETS and lung function responses in the asthmatic subjects, they reported that "not all subjects showed the same pattern of pulmonary responses to the smoke exposure." The authors also reported that "we were not able to exclude the possibility that these changes in pulmonary function were emotionally related to cigarette smoke" [emphasis added]. Similarly, the 1986 Surgeon General's report recognized that "in this study, subjects were not blinded as to the exposure and were selected because of complaints about smoke sensitivity."

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- OSHA also references a 1991 review article by Stanton Glantz and Richard Daynard (Tobacco Liability Project) which makes several claims regarding exposure to environmental tobacco smoke, none of which is supported by a thorough and critical review of the scientific literature available. [Ex. 3-438D]

- OSHA claims that asthmatics are believed to be especially sensitive to various environmental influences, including ETS, but a thorough review of the scientific data on ETS does not convincingly support this contention.

- There are currently ten major studies on ETS exposures among adult asthmatics. Seven of the studies are clinical in nature, where exposures to ETS were controlled under laboratory conditions. The other three studies are population surveys. All of the studies evaluate reports of respiratory symptoms such as coughing, wheezing, and irritation ("subjective complaints") and changes in lung function (an "objective" test for lung impairment).

- Only two of the seven clinical studies report objective decreases in lung function among the majority of asthmatics exposed to environmental tobacco smoke. However, the patients in both positive studies were exposed to excessively high and unrealistic levels of ETS, and, as mentioned above, the

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authors of one of the studies conceded that the observed effects may have been due to psychological factors. In the remaining five clinical studies, a number of patients reportedly complained of subjective symptoms upon exposure to ETS, but objective results (i.e., evidence of airways obstruction or significant changes in lung flow rates) were not observed in the vast majority of patients.

- Data from the three population surveys on adult asthmatics are generally consistent with data reported in the majority of clinical studies. A report of a large-scale population survey in the U.S. suggested that ETS exposures in the home did not affect either symptoms or pulmonary function in adult asthmatics. Another group of U.S. researchers recently reported that exposure to ETS did not impair lung function in the 263 asthmatic adult subjects studied. The third study reported mixed results for the development of asthma-related symptoms in individuals reporting exposures to ETS during childhood and adulthood.

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- **OSHA fails to discuss the problems in generalizing data from "exposure chamber" studies to the "real-world" situation.**

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- The conditions under which asthmatic patients are exposed to ETS in these studies are of questionable relevance to "real-life" exposures.

- The Surgeon General, in the 1986 report on ETS, conceded that exposure chamber studies may not be indicative of the "real world" situation:

> Acute exposure in a chamber may not adequately represent exposure in the general environment. Biases in observation and the in [sic] selection of subjects and the subjects' own expectations may account for the widely divergent results. Studies of large numbers of individuals with measurement of the relevant physiologic and exposure parameters will be necessary to adequately address the effects of environmental tobacco smoke exposure on asthmatics.

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- **The majority of animal studies referenced by OSHA are studies of mainstream tobacco smoke and are not relevant to a discussion of potential pulmonary effects in nonsmoking adults exposed to environmental tobacco smoke in the workplace.**

- Although OSHA refers to the studies in this section as experimental "ETS" studies, the majority of the studies are mainstream smoke studies which have little or no relevance to

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ETS issues because ETS is not the same as either mainstream or sidestream smoke.

- OSHA mentions isolated conclusions from several experimental animal studies but makes no attempt to explain how these data relate to real-life ETS exposures of nonsmoking adults in the workplace. OSHA also does not make any attempt to explain the physiological or clinical significance, if any, of the reported data. Nor does OSHA address the apparent inconsistencies in the reported data. For example, "effects" may be reported in one species but not in another.

- OSHA makes no attempt to explain the relevance, if any, of these high-dose experiments in animals to real-life workplace exposures in humans, even when some of the studies from which they report data acknowledge that these exposure levels are extreme when compared to the "real world" of "smoke-filled" restaurants or offices. OSHA's responsibility in this proposed rulemaking is to show that workplace exposures to ETS are likely to result in material health impairment in non-smoking adults. They have failed to substantiate this claim.

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- **Overall, OSHA fails to reference much of the relevant literature submitted in response to the OSHA RFI in 1992.**

- **OSHA presents no critical discussion of potential confounding factors, merely stating that the studies "varied" in their consideration of such factors and that "several studies" have examined isolated variables; OSHA makes no statement regarding the adequacy of control for such factors in these studies.**

- The Proposed Rule presents selected data on the possible association between exposure to ETS and decreased pulmonary function in adult nonsmokers. Philip Morris submitted much of the literature which OSHA has omitted from its Proposed Rule to the docket for the RFI in 1992. [Ex. 3-1074]

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- **OSHA, while conceding that the studies on ETS exposure and pulmonary effects in nonsmoking adults "vary by numerous factors," makes no apparent attempt to explain why these variations are given no importance in their "analysis" of the literature.**

- OSHA does not elaborate on its statement that the studies on ETS exposure and respiratory effects in nonsmoking adults

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"vary by numerous factors, such as the population studied, the measures used to estimate exposure to ETS, and the physiologic and health outcomes examined."

- While other reviewers of this body of literature have concluded that it is difficult, if not impossible, to make any definitive conclusions from these data, OSHA attempts, but fails, to make a case for causation.

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REPRODUCTIVE EFFECTS

- **OSHA'S Proposed Rule lacks consistency in its definition of "ETS exposure during pregnancy."**

- In some instances, OSHA appears to be discussing the potential effects on the fetus that may be associated with active smoking of the mother during pregnancy. At other times, the authors of the Proposed Rule are discussing ETS exposure of the mother during pregnancy.

- Active smoking of the mother during pregnancy is not synonymous with ETS exposure. OSHA's task is to show that there is a significant risk of material health impairment in

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fetuses whose mothers are exposed to ETS at work during their pregnancies.

- **The studies referenced by OSHA which examine active smoking during pregnancy are irrelevant to this discussion.**

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- **OSHA provides a brief, selective and seemingly irrelevant discussion regarding the possible association between workplace ETS exposures of nonsmoking pregnant women and various adverse reproductive outcomes.**

- OSHA claims that "other reproductive effects that have been ascribed to maternal ETS exposure include miscarriage, an increase in congenital abnormalities, and numerous other physiological effects." [59 FR 15979] As references for this section, OSHA provides citations to the Taylor and Wadsworth (1987) study. [Ex. 8-299] This study examined active maternal smoking and reported no data on ETS exposures during pregnancy.

- OSHA also cites a response to a Letter to the Editor by Ira Tager. [Ex. 8-297] In this letter, Tager makes no mention of "other physiological effects" in infants born to mothers

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reportedly exposed to ETS during pregnancy and states the following regarding this issue:

> In discussing the harmful effects of passive smoking [during pregnancy], it is important to point out that there is no body of data that absolutely proves that harmful effects will be experienced.

- OSHA also claims that "the effects of environmental [tobacco] smoke exposure on the fetus may have long-term sequelae into childhood and adulthood." [59 FR 15979] The first three studies cited by OSHA make no mention of any purported "effects" of ETS exposure during pregnancy on the fetus. [Exs. 8-53, 8-181, 8-213]

- The fourth study cited by OSHA is a study of active maternal smoking during pregnancy. [Ex. 8-225] OSHA also references a CDC survey which provides no information, conclusions, or data regarding the possible effects of maternal ETS exposure during pregnancy. [Ex. 8-51] Finally, OSHA again cites the response to the Letter to the Editor by Ira Tager outlined above. [Ex. 8-297]

- OSHA states that exposure to ETS may be "reflected in the growing child as reductions in lung development" and that "this is especially relevant if that child continues to be

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exposed to ETS throughout childhood and into adulthood." [59 FR 15979] OSHA again references the Tager letter above to support this point. [Ex. 8-297]

- It also cites a paper which reports:

> Paternal smoking does <u>not</u> appear to be the environmental exposure leading to both childhood respiratory illness and adult chronic air-flow limitation. [Emphasis added; Ex. 8-177]

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- **OSHA does not provide a balanced and complete discussion of the literature available, i.e., OSHA fails to mention studies which report no association between exposure to ETS during pregnancy and adverse reproductive outcomes.**

- In 1992, one group of researchers examined the issue of maternal ETS exposure during pregnancy and spontaneous abortion (miscarriage). Although the authors reported that paternal smoking was not associated with spontaneous abortion (after consideration of other independent risk factors), exposure to ETS from sources other than the father was reportedly associated with an increased risk of miscarriage. This is surprising considering that fact that the authors

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observed no excess risk of spontaneous abortion among "moderate" smoking mothers or among those who actively smoked an average of more than 20 cigarettes per day in the first trimester. The inconsistent and contradictory data from this study appear to be the result of inadequate control for other factors.

- Other research has suggested possible associations between maternal exposure to ETS during pregnancy and infant size, premature labor and neonatal asphyxia.

- In contrast, Savitz, et al., reported that they could provide "no definitive evidence" of an association between paternal smoking and any birth defect. Other authors similarly have reported no associations between maternal exposure to ETS during pregnancy and the incidence of heart defects, premature rupture of amniotic membranes, strabismus (an eye disorder) and various other birth defects.

- Although several isolated studies have suggested an association between reported exposures to ETS during pregnancy and various conditions in the infant, the data must be considered both inconclusive and, in the words of one scientist, "controversial." Another author has suggested:

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Much remains to be done in order to determine whether ETS has any effect on human reproduction or development. Improvements in design of epidemiologic studies of ETS effects, particularly in the areas of exposure assessment and validation and elimination of confounders, are especially important. In addition, appropriate animal studies would be helpful in allowing definitive conclusions to be drawn.

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- **Despite the irrelevance of much of the literature OSHA cites, OSHA still fails to provide a critical discussion of the problems inherent in such epidemiological studies.**

- Probably the most important problems in epidemiologic studies are the lack of quantitative exposure data and the lack of adequate control for potential confounding factors.

- Exposure estimates in these studies are based on questionnaire information, the validity of which have been questioned repeatedly in the scientific literature.

- OSHA conveys the impression that confounding factors have been adequately ruled out in these studies.

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- OSHA fails to mention data which, after being adjusted for other factors, have failed to reach statistical significance. The control of confounding variables is of extreme importance in ETS studies examining birth weight. ETS exposure has been shown to "correlate positively with a number of known determinants of decreased birth weight," including lower socioeconomic status and poor nutrition.

- Another group of authors suggests that "it is generally believed that birth weight, perinatal mortality and other measures of reproductive health are sensitive markers of social conditions."

- OSHA claims that confounding factors have been adequately ruled out as an explanation for the reported association between paternal smoking and reductions in infant birthweight. OSHA mistakenly arrives at this conclusion by taking factors that were controlled for in a few of the studies and generalizing to the entire population of studies.

- In addition to these general problems, there are problems specific to the studies OSHA chose to cite in its Proposed Rule. For example, to support its statement that "data on the reproductive effects due to the exposure of nonsmoking pregnant women to ETS has been presented in many studies,"

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OSHA references two abstracts and six papers. [Exs. 3-438, 8-92, 8-174, 8-208, 8-273, 8-285, 8-287, 8-299] A complete review of the statistical procedures and methods, let alone the data, cannot be performed on abstracts.

- There are also problems specific to several of the papers cited by OSHA.

- The Martin & Bracken paper reported that women who were reportedly exposed to someone else's cigarette smoke for at least two hours per day, either at home or at work, during pregnancy delivered infants that were, on average, 24 grams lighter than the infants of women who were reportedly not exposed to ETS. [Ex. 8-208] This relationship was not statistically significant. This paper is also used to provide support for OSHA's statement that "passive exposure to tobacco smoke is estimated to double the risk of low birthweight in a full-term baby." [59 FR 15979] While the authors reported a relative risk of 2.7 (95% confidence interval 1.05-4.50) for a subgroup of the women, when all women with full-term deliveries were included in the analysis there was no statistically significant relationship between reported exposure to ETS during pregnancy and a reduction in infant birthweight.

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- As one author wrote in 1990:

> The analyses reported by Martin and Bracken (1986) are inconsistent and difficult to interpret. This may be due, at least in part, to the authors' use of a relatively crude estimate of ETS exposure. Their findings would have been more meaningful if further information had been available regarding exposure intensity and duration. Further, since questionnaire data were solicited early in gestation, intensity and duration of ETS exposure may have changed considerably for a number of subjects over the remainder of pregnancy.
>
> Potentially important confounders, such as maternal weight and the child's sex, were apparently not determined during the data collection, and thus were unavailable for the analysis, although such variables may significantly influence birth weight.
>
> It is puzzling that the authors used statistical significance as the criterion for inclusion of potential confounders in their multiple regression analyses when, according to various experts, this may eliminate important confounders (e.g., because of low statistical power or multicollinearity).

- It should not, then, be surprising that Martin and Bracken conceded that "whether the association found [between decreased infant birthweight and ETS exposure during pregnancy] is due to passive smoking or to some other related factor is unclear" [emphasis added].

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- The Rubin (1986) paper reported that each pack of cigarettes smoked by the father each day during a mother's pregnancy was associated with a 120 gram reduction in the offspring's birthweight. [Ex. 8-273] However, even a reviewer who is critical of parental smoking, Trichopoulos, has stated that the reported reduction in birthweight reported by Rubin was "extraordinarily large" probably because of poor control for confounding factors.

- Similarly, another author wrote the following regarding the 1986 Rubin paper:

> An ETS effect of this relative magnitude seems improbable, however, when the relative degrees of exposure are considered. Moreover, in their regression analysis of paternal smoking effects, the authors failed to include interaction terms. This is true even though they reported finding a significant interaction between social class and paternal smoking effects, and earlier studies had reported interactions between effects associated with maternal and paternal smoking status. Rubin and coworkers failed to control for a number of other potential confounders as well.

- A study which reports the following is also cited by OSHA:

> We report <u>negative results</u> on induction of chromosomal damage in 2 separate groups of intensive involuntary exposure to tobacco smoke, non-smoking restaurant personnel and

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newborn children of smoking mothers. [Ex. 8-287; emphasis added]

- Finally, the other study cited by OSHA is a paper on the possible effects of active smoking by the mother during pregnancy. [Ex. 8-299] The paper contains no data on pregnant mothers who are exposed to ETS in the workplace during pregnancy.

- OSHA fails to discuss a number of other studies which have reported no statistically significant associations between maternal exposure to ETS during pregnancy and the delivery of low birthweight infants. In fact, one study considered 57 different risk factors for low birthweight infants and reported that paternal smoking (as an index of exposure to ETS) had no statistically significant effect on infant birthweight.

- OSHA does not provide a detailed discussion of the clinical significance, if any, of the reported decrements in infant birthweight allegedly associated with ETS exposure of the mother during pregnancy.

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- **OSHA's claim that prenatal exposure to ETS and exposure to ETS as a child may increase an individual's cancer risk by a factor of two is unsupported by a thorough review of the available literature.**

- In an attempt to substantiate its claim regarding the possible risk of cancer in nonsmokers exposed either prenatally or as a child to ETS, OSHA cites three papers. [Exs. 8-65, 8-164, 8-252]

- The first study reported an association between exposure to maternal smoking during childhood and an increase in lung cancer risk in nonsmokers in only one subgroup of subjects. Janerich et al., 1990, reported only one statistically significant risk estimate out of 13 exposure categories.

- The third reference is a reply to a Letter to the Editor regarding the Pershagen 1987 study (which itself is not referenced by OSHA). [Ex. 8-252] The Pershagen study reported "no consistent evidence of an effect," and the 95% confidence interval encompassed 1.0 for both histologic groups. Therefore, the studies' risk estimates were not statistically significant.

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- The two studies and the Letter to the Editor cited by OSHA examine the potential effect on an individual's cancer risk from exposure to parental smoking during childhood. These studies are therefore irrelevant to a discussion of potential health effects on the fetus from exposure of the mother to ETS in the workplace during her pregnancy. Nonetheless, a reviewer of this literature concluded that "the data do not indicate any association at all between risk of lung cancer in never smokers and exposure to ETS at work, or in childhood."

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- **OSHA provides a reference to one experimental animal study which it claims is supportive of the contention that exposure of pregnant mothers to ETS in the workplace presents a significant risk of material health impairment to the fetus.**

- Although OSHA acknowledges that "experimental research on the adverse reproductive effects associated with ETS exposure in animals is limited," they do report on one study. [Ex. 8-6] This study reported that sciatic nerve tissue taken from the offspring of ETS-exposed female mice revealed "definite toxic effects" on the neonatal tissue.

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- There are several limitations of this study. Probably the most important is the small sample size. The authors reported data on only six exposed offspring and six controls. In addition, COHb levels of the exposed pregnant mice were 9%, which the authors report is "equivalent to that found in humans who actively smoke 10-20 cigarettes per day." As one author suggested, studies which simulate mainstream smoke and employ levels equal to or greater than those expected from active smoking generate data which "are not appropriate for assessment of the likelihood or nature of ETS effects." The author also suggested that the authors of such studies should realize that "careful attention must be given to ensure that observed effects are not simply the result of maternal toxicity and systemic stress resulting from excessive doses."

- The authors of this study themselves also noted that these reported changes have been observed in other studies, including studies of the diabetic strain of the C57BL/KsJ mouse and in studies of decreased maternal food intake. They concede that "the irregularities noted in our investigation could be attributed to causes other than cigarette smoke inhalation as previous studies demonstrate."

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GENOTOXICITY

- **OSHA fails to justify its inclusion of genotoxicity as a separate category under the major heading of "health effects"; OSHA fails to show that genotoxicity is a material impairment to health.**

« Genotoxicity refers to damage to DNA (the hereditary material). Permanent, heritable changes in the DNA are called mutations, and may be examined in tests for mutagenicity, such as the Ames test, in which mutation rates are measured in a particular strain of bacteria. Some correlations have been made between mutagenicity and carcinogenicity (the ability to induce cancer).

- All forms of life are constantly exposed to physical and chemical agents in the environment (e.g., radiation) and to endogenous (internal) agents with the ability to cause changes in DNA. DNA has been called an "unstable" molecule, and it has been noted that endogenous DNA damage may occur at the rate of 10,000 base pairs per cell, per day.

- According to Bruce Ames, developer of the Ames assay for mutagenicity, human exposure to potentially mutagenic or carcinogenic substances is much greater than generally

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appreciated, e.g., the environment can be thought of as "filled with potential carcinogens."

- Moreover, conclusions about genotoxicity obtained from in vitro systems, while certainly providing some information about the substance being tested, must nevertheless be put into the proper biological context. The magnitude of a genotoxic response in the whole organism may be substantially different than that observed in a bioassay. As Ames and Gold noted:

> [H]umans have numerous inducible defense systems against mutagenic carcinogens, such as DNA repair, antioxidant defenses, glutathione transferases, and so forth . . . [L]ow doses of carcinogens appear to be both much more common and less hazardous than is generally thought.

- Given the ubiquity of mutagens in the environment and the existence of numerous "defense systems" against mutagens, OSHA has not provided sufficient information in the Proposed Rule to support its treatment of genotoxicity as a "health effect" or to establish genotoxicity as a material impairment to health.

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- **OSHA's review of the literature on the claimed genotoxicity of ETS is incomplete; a review of additional relevant studies provides no support for OSHA's claim.**

- OSHA's discussion of genotoxicity begins with a series of statements about the claimed correlations between genotoxicity and carcinogenicity. [Section II.C.7., 59 FR 15981] OSHA fails to provide references in support of these statements, although they appear to be OSHA's justification for discussing genotoxicity.

- The Proposed Rule then contains a discussion of a number of studies in which cigarette smoke or cigarette smoke condensate was tested in the Ames Salmonella typhimurium assay, and an increased mutation rate was reported.

- OSHA omitted at least one relevant study from this discussion in the Proposed Rule. In 1991, Bombick, et al., reported on a cellular smoke exposure techniques using rat liver cells and the Ames Salmonella assay. After a three-hour exposure using ETS at a concentration of 1.5 mg total particulate matter/m, the authors report:

> Using the neutral red cytotoxicity and Ames mutagenesis assays there were no differences observed in the ETS-exposed cells and their

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> respective room air controls, indicating that ETS was biologically inactive as tested. [Emphasis added]

- The Proposed Rule also discusses studies reporting that various constituents and extracts of ETS collected from indoor air are capable of inducing mutations in the Ames assay are also discussed. [Exs. 4-202, 4-5, 4-198, 4-201, 4-203] However, the significance of such reported findings has not been established. Virtually all air samples, whether in the presence or absence of smoking, can be shown to be mutagenic in various bioassays. Indeed, no substance, including foods and natural materials, has been unequivocally shown to be free of mutagenic and/or carcinogenic properties.

- Of relevance, a study not cited by OSHA has reported that sidestream smoke exhibits reduced activity as it ages and becomes diluted, that is, as it becomes ETS. Sonnenfeld and Wilson report on an experiment in which cultured mouse fibroblast-like cells were exposed to mainstream or sidestream smoke of various ages. Based on their data on cytotoxicity (cell mortality), the authors write:

> Aging of SS smoke resulted in a rapid decline in the mortality generated by the smoke. As calculated from the linear regression curve, an increase in age of SS smoke of 30 s after

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generation would have resulted in a total loss of cytotoxic effects. [Emphasis added]

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- **The Proposed Rule almost completely overlooks genotoxicity studies using bodily fluids of persons exposed to ETS; these data do not allow a conclusion about genotoxicity to be reached.**

- One area of research essentially overlooked in OSHA's Proposed Rule comprises those studies that have compared the mutagenicity of body fluids of nonsmokers exposed to ETS and nonsmokers not exposed to ETS. Several of these studies report no significant difference in mutagenic activity. [Ex. 8-152]

- For instance, in research by a team of German researchers, ten nonsmokers were exposed to ETS, generated by human smokers, for eight hours under two exposure conditions. The two experiments were characterized by CO levels of 10 ppm and 25 ppm, respectively; according to the authors, both exposure regimes represent higher exposures than "real-life" situations. Elsewhere, they described Experiment 2 as "far from being realistic," and bearing "no relation to a real-life

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situation." In addition, the authors controlled for the effect of mutagens from the diet by keeping their subjects on a diet low in polycyclic aromatic hydrocarbons. Urine samples from both smokers and nonsmokers were tested in the Ames Salmonella assay. The authors report:

> All urine extracts of ETS exposed non-smokers were found to be negative in the mutagenicity test when applying the [criterion] of Ames (doubling of spontaneous mutation rate).

- **Thus, even at exposure levels higher than would be expected on average, no increase in mutagenicity could be measured. These data do not support claims that ETS exposure is associated with an increase in mutagenic activity.**

- Citing the high variability of measures of urinary mutagenicity and questions about the relevance of increased urinary mutagenicity to cancer risk, the authors write:

> These considerations lead to the conclusion that measuring the urinary mutagenic activity, at least in passive smokers, is not an appropriate method of predicting an increased risk to human health.

- The authors also say:

> The data suggest that nonsmokers in real-life situations take up very low doses of ETS

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constituents, and detoxification of the genotoxic substances inhaled is effective.

- **And:**

> Whether ETS exposure can lead to an elevated urinary mutagenicity is a matter of controversy. In most investigations no significant increase has been observed. . . .
>
> In our experience, the Ames test for detection of urinary mutagenicity is far too insensitive to assess such a low exposure. The results of our investigations, as well as those of other authors, suggest that urinary mutagenicity, which would be a potential marker for ETS particle exposure, remains unchanged after ETS exposure.

- The few studies reporting statistically significant increases in urinary mutagenicity among individuals exposed to ETS did not employ realistic levels of exposure to ETS, and they did not control adequately for the presence of mutagens in the diet of the study subjects.

- For instance, in the Bos, et al., study, the exposure condition consisted of the smoking of 157 cigarettes over six hours in a room with "poor ventilation." The relevance of such an exposure to "real-life" conditions is certainly questionable. With respect to diet, Bartsch, et al., acknowledge, concerning their study, that

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Urinary mutagenicity is influenced also by dietary habits; although we collected information on diet, the dimension of the study (particularly as far as passive smokers are concerned) does not allow adequate statistical treatment of this potential confounding factor.

- Other related studies have examined levels of various DNA changes in nonsmokers exposed to ETS. [Exs. 8-152, 8-287] Based on the data presented in these studies, nonsmokers exposed to ETS do not appear to exhibit increased DNA adduct formation, nor do studies report increased levels of chromosomal changes in cells of nonsmokers exposed to ETS. Discussion of these studies follows.

- Collman, et al., collected data from 16 nonsmokers, 15 "passive smokers" (currently living with one or more smokers), and 13 current smokers, all women. Sister-chromatid exchange (SCE) frequencies in lymphocytes (a type of white blood cell) were compared with and without coincubation with a chemical that enhanced the frequency of SCEs. Based on both assays, the authors report that "the frequency of SCEs in persons passively exposed to smoke was not higher than in nonsmokers."

- In a report by Husgafvel-Pursiainen, peripheral blood lymphocytes were examined for SCE frequency. Study groups consisted of 12 smoking waiters and waitresses, 20 nonsmoking

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waiters and waitresses who were occupationally exposed to ETS, and 14 nonexposed office workers. The author reports that "[t]he mean SCE level in exposed non-smokers did not differ from that observed in the non-exposed group." Although no ETS measurements from the restaurants were reported, the author characterizes them as "heavily polluted," and the exposure as "long-term." This study, which reports data from persons exposed in a "real-life" situation, does not support claims of the genotoxicity of ETS.

- Chromosomal aberrations (CAs) and SCEs were examined in peripheral blood lymphocytes from nine smoking waiters, 16 nonsmoking waiters exposed to ETS at work, and 7 reportedly nonexposed nonsmokers by Sorsa, et al. [Ex. 8-287] The authors report that "[n]o significant differences were seen between the groups or subgroups in the 2 parameters." Thus, no "genotoxic" effects could be detected in persons exposed to ETS at "real-world" levels.

- Holz, et al., report that DNA adduct levels were compared in monocytes (a type of white blood cell) of smokers and "heavily exposed passive smokers," who had been exposed in a chamber. DNA adducts above background were reported in smokers; they disappeared in less than 40 hours. The authors report no

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above-background adduct levels in study subjects exposed to ETS.

- In a study by Gorgels, et al., 50 self-reported ETS-exposed men ("passive smokers"; average 72.8 hours exposure per week) were compared with 56 self-reported low ETS-exposed men (average 5.1 hours per week). SCEs in cultured lymphocytes were examined; the authors reported that "[n]o difference was observed between low exposed non-smokers and the passive smokers." They concluded:

> Our results are in accordance with previous smaller studies in less homogeneous populations of non-smokers. These studies also failed to demonstrate even a tendency for an association between passive smoking and SCE levels. . . .

- Five male smokers, five male nonsmokers, and five male nonexposed nonsmokers were compared in Holz and colleagues' 1993 paper. The endpoint examined was DNA single-strand breaks (SSBs), "considered to be an important parameter of genotoxic stress," in lymphocytes. The authors write:

> All probands revealed measurable and varying SSB levels. Since DNA is an unstable molecule and estimated endogenous damage exceeds 100000 affected base pairs per cell per day, we assume that SSB base levels reflect unrepaired lesions. Active smoking caused an increase in

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SSBs in peripheral blood lymphocytes. This effect could not be found in passive smokers . . .

- ETS exposure in this study consisted of five smokers each smoking 24 cigarettes in eight hours in an exposure chamber. This study provides no support for claimed genotoxic effects of ETS, even at a high exposure level.

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- **Concluding remarks.**

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